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PRESIDENTIAL ADDRESS*

By JONATHAN C. MEAKINS, F.A.C.P., *Montreal, Quebec, Canada*

IT has been a custom of our College for the President to address you at least once a year and to take this occasion to deal with activities of the College, and incidentally such other subjects as it may please him to choose. Before proceeding with these matters I wish to take this opportunity of expressing my appreciation of the honor conferred upon me last year in electing me your President. Not only is it a great distinction to be chosen for this position by one's fellows in Internal Medicine, but also to be deemed worthy to follow in the footsteps of a lengthening line of America's most distinguished physicians. I sincerely thank you and hope that during my trusteeship the affairs of the College have not suffered.

The excellence of our Annual Clinical Meetings requires no eulogy from me. The taste we have had of the fare which Dr. Stengel and his committees have provided for us, speaks for itself. There is only one criticism, but hardly that, let me say complaint, that I might lodge. As each year passes our programs carry us to higher and higher heights in the medical stratosphere, and if we do not find some means of protection the concentration of the intellectual cosmic rays may consume us.

This Nineteenth Annual Clinical Session has, if possible, exceeded our anticipations of what such a meeting could be in Philadelphia. So I wish to express to Dr. Stengel and all of his colleagues our deep appreciation of the intellectual and social hospitality which they have provided for us. It has been indeed not only abundant and choice, but gracious. Our Annual Meetings are always most pleasant, particularly in renewing old friendships and making new ones. In particular, I take pleasure on this occasion in extending to the newly elected Fellows the friendly hand of welcome with the sincere wish that they will derive inspiration from their associations within the College. We must always remember that *we* are the College, and its success, reputation, and ideals are dependent upon the efforts and aspirations of one and all of us. The Board of Regents and the Board of Governors are but elected servants of the College. The success of our organiza-

* Read at the Philadelphia meeting of the American College of Physicians, May 1, 1935.

tion must depend upon the combined efforts of all as individuals and not upon the idealism of the few. The College has a great future but the steady progress toward its goal is the responsibility of each one of us. We must think as to where we are going and what is its eventual destiny. But more of this anon.

The joy of our yearly reunions is always tinged with a sadness for the absence of those who will be with us no more. Many we have called 'friend' and admired for their contributions to the progress of our profession and welfare of mankind. Others we had known but a short time but had hopes for greater intimacy and that personal association which binds the heart, the mind and the hand. I desire, on behalf of us all, Masters, Fellows, and Associates, to express our deep and sincere sympathy to the families and friends for their sad loss, and to assure them that wounds caused by the absence forever from our midst of our revered colleagues will only be healed by the Greatest of all Physicians.

It is now my duty to review in brief some of the activities which have occupied your Officers and Board of Regents since our meeting last year in Chicago. It is gratifying to record that the financial position of the College is one of solidity and is steadily improving. For this we are indebted in great part to the sagacity of our Treasurer and the Finance Committee, but also in an equally great part to our ever-watchful Executive Secretary, Mr. Loveland, and his Staff, who by economy and excellent executive ability have guided our ship through the contrary winds and tempestuous seas of these trying years. To him I wish to express our sincere thanks and appreciation for his fidelity to the interests of the College.

Our official journal, the ANNALS OF INTERNAL MEDICINE, has been under the capable guidance of the editor, Dr. Pincoffs, ably assisted by the Editorial Board. His task has not been an easy one. The duties of an editor I often think are the most exacting that can fall upon the shoulders of anyone. They require unremitting vigilance in so many directions; not the least of which is the selection of a comparatively few papers from so many offered: all of which must be carefully read and then assessed and balanced as to their acceptance. All are not equally suitable although excellent. He has a certain biblical rôle to play,—to paraphrase—"Many are offered but few can be chosen." I know it well, and it must be so; not that I have ever been an editor, but I have suffered by them, and on second thoughts I have seldom found them wrong. Writers, like artists, are apt to be touchy about the quality of their creations. Although these difficulties are a worry to the editor I am sure they are insignificant compared to the exasperations of delayed and changed galley proof and the lamentations and vituperations of the publishers. He, poor man, is between the upper stone, —the fond and temperamental parent of the manuscript, and the nether one,—a cold and profit-exacting printing press. But I am sure we all have confidence and first-hand knowledge that our Editor is serving the Annals excellently and for this we thank him.

Turning now to more general matters, one cannot dismiss the effect of the world-wide social turmoil of the past five years. Continents, nations and governments have been more or less blindly groping through a fog of shattered principles that appeared a short time ago to have been as firm as the rock of Gibraltar. It would be beyond the realm of possibility that our medical world would have escaped unscathed. Several of my predecessors have dwelt on certain aspects of this matter and it is not my purpose to deal with it at any length; but, certain phases have developed during the past year which must be, at least briefly, referred to. In the first place it must not be overlooked that our College is an international body. We are Fellows together for mutual help and guidance and the experience from experiments in one country or section may be of help to another, when not offered in any spirit of superiority but in a courteous and understanding manner as between friends. This is a vast continent and the problems of congested cities as compared with those of the farm, of the seaboard as compared to those of the great mid-land, have a greater divergence between the East and West than they have between the North and South of this continent. From whichever region we come, we must always cultivate a kindly and sympathetic appreciation of each other's difficulties.

Some six months ago your President, Mr. Roosevelt, in his wisdom, appointed a Medical Advisory Committee under the Committee on Economic Security, to study and advise on intricate and difficult problems which would naturally arise under any system of health insurance or other medico-social plan. I wish to inform you that the College happened to be well represented on this Committee by three members of the Board of Regents, not as College officials but entirely, I am sure, on account of their well merited reputation of being wise councillors in all matters which touch the honor and rights of the medical profession and our ageless trust, the welfare and health of all peoples. I merely touch on this matter here to assure you that the Board of Regents are not unmindful of the present trend of social affairs and are fully alive to the percussions they may have on the practice of Medicine. It would be presumptuous of me to make further comment, so here I leave the matter in the competent hands of my successor.

After these general remarks I wish to pass on and consider seriously certain matters which to my mind are of urgent concern at this moment. I am sure that many of us, from time to time, ask ourselves what the American College of Physicians really stands for and what its destiny should be. When we take stock, we can with pride point to our Annual Clinical Meetings and to our Journal which has a high standing among those devoted to the practical or clinical aspects of our profession. But, if we become a little more introspective and analytical, we must acknowledge that other associations and societies also have such meetings and publications for the broadcasting of their scientific and clinical erudition. Some of these are more exclusive than others. This exclusiveness, of course, is their own affair, undoubtedly determined by their policy, their ideals and their ob-

jectives. As Dr. Vincent so cleverly, but withal wittily, told us in Boston in 1929, there are different standards or criteria whereby the " elite " may be judged. We, by our very name—" The American College of Physicians " —have abrogated to ourselves a certain aristocratic position or an " eliteness," if I may use the word, which we must justify in the eyes of the rest of the profession. We call ourselves a College established primarily for the enrollment of " internists " or those of the medical fraternity or guild who devote themselves entirely to the profession of Medicine, as it is commonly known, to the exclusion of other methods of diagnosis and treatment. Was such a movement necessary? And if so, why? And if these answers can be found satisfactory are we carrying it out in the proper manner or are we but another, rather exclusive and expensive, medical society?

To these questions I shall attempt to give answers and at the same time show, as I see it, a road upward to a bigger and better future for this College in and for which we have both faith and affection. To do this I must ask you to bear with me for a short period while I review as briefly as I may certain historical events which I am sure you will find as pertinent today as they were in the distant past.

If we search through the Acts and Ordinances of the fifteenth century in Great Britain we find in the reign of Henry VI, to be exact, 1460, a Royal Edict securing benefits and monopolistic rights to the Barber-Surgeon. The exact reasons are not stated but presumably their prerogatives were being encroached upon by those whom they considered unfitted to practice the art, —in other words, the unqualified surgeons of the day. This edict appeared to satisfy the London Barbers for nigh on one hundred years.

In the meantime, the Surgeons in Edinburgh seem to have been in a bad way. The country was in anarchy and chaos; the Barons were more powerful than the King (James IV); the people were oppressed and all forms of rascality ran riot. The Surgeons, finding their profession invaded by all and sundry, petitioned the Town Council of Edinburgh to grant them an exclusive monopoly. This was done in 1505 and was termed a " Seal of Cause " and confirmed in the following year by the Royal Authority. Many decades pass without further mention of the activities of this craft. They appeared to be the sole teachers and almost the sole practitioners in the city. In 1589 they condescended to admit barbers to their corporation but these could not practise surgery or have any voice in the deliberations of their guild. They had, indeed, exclusive privileges but these were being encroached upon by two descriptions of practitioners, the unqualified physicians and the unqualified apothecaries. The former petitioned Cromwell to give them by means of a patent, power to elect themselves into a College, not merely for Edinburgh but for all Scotland. They wished also to have power of examining and licensing apothecaries, of visiting the drug shops, and enforcing their authority. It must be appreciated that the physicians of that day in Scotland were few and for the most part held foreign degrees. The only Scottish University granting a medical

degree was St. Andrews. The surgeons and apothecaries were alike in great alarm and scurried for safety by inducing the Town Council to constitute a Brotherhood (sic) of Apothecaries and Chirurgeon Apothecaries. The surgeons did not soon forget this attack on their monopoly and exerted every effort to maintain their exclusive rights, even fighting the University or Town College as well as the physicians.

We shall now return to London where the surgeons and barbers were apparently living in peace, but all was not well with the practice of the healing art. This I think is best appreciated from " An Act for the appointing of Physicians and Surgeons " in the third year of the reign of Henry VIII (1512). It reads in part as follows:

> " To the King our Sovereign Lord, and to all the Lords Spiritual and Temporal, and Commons in this present Parliament assembled: forasmuch as the science and cunning of Physick and Surgery (to the perfect knowledge whereof be requisite both great learning and ripe experience) is daily within this Realm exercised by a great multitude of ignorant persons, of whom the greater part have no manner of insight in the same, nor in any other kind of learning: Some also can no letters on the book, so far forth that common artificers, as Smiths, Weavers, and Women boldly and accustomably take upon them great Cures, and things of great difficulty; in the which they partly use Sorcery and Witch-craft, partly apply such Medicines unto the disease, as be very noious, and nothing meet therefore, to the high displeasure of God, great infamy to the Faculty, and the grievous hurt, damage, and destruction of many of the King's liege people; most especially of them that cannot discern the uncunning from the cunning; Be it therefore (to the surety and comfort of all manner people) by the authority of this present Parliament enacted, That no person within the city of London, nor within seven miles of the same, take upon him to exercise and occupy as Physician or Surgeon, except he be first examined, approved, and admitted by the Bishop of London, or by the Dean of Pauls, for the time being, calling to him or them four Doctors of Physick, and for Surgery, other expert persons in that Faculty; and for the first examination such as they shall think convenient, and afterward alway four of them that have been so approved."

And so on with due fines of five pounds for each month of illegal practice. It allows Bishops in other dioceses outside of London to approve also but only after proper examination; " Provided alway, that this Act nor anything therein contained, be not prejudicial to the Universities of Oxford or Cambridge." There is also a memorandum " That Surgeons be comprised in this Act as Physicians."

It will be noted that this but enacts how the privilege of practising Medicine should be obtained and who should grant it.

At this time the great Thomas Linacre was physician to Henry VIII

and the foremost physician of his time. The life of Linacre is not part of our present thesis. One of his great labors alone interests us, namely, the creation of the Royal College of Physicians of London. He undoubtedly got the idea during his period in Padua where he obtained his Doctorate of Physick with applause. The organization and ideals were his own as was also the great part of the expenses; the gift of the Crown was limited to the grant of the letters patent. "The wisdom of Linacre's plan speaks for itself. His scheme without doubt was not only to create a good understanding and unanimity among his profession, which of itself was an excellent thought, but to make them more useful to the public; and he imagined that by separating them from the vulgar empirics and setting them upon such a reputable foot of distinction, there would always arise a spirit of emulation among men liberally educated, which would animate them in pursuing their inquiries into the nature of diseases, and the methods of cure, for the benefit of mankind; and perhaps no founder ever had the good fortune to have his designs succeed more to his wish."

Linacre's efforts were undoubtedly crowned by the creation of the first real College of Physicians or Surgeons in either England, Scotland or Ireland. Companies or Guilds of Surgeons or Barber Surgeons certainly preceded this College but they were not founded on the same ideals for the advancement of learning. These ideals were emulated by others but all must pay tribute for the inspiration to such lofty thoughts. I shall not weary you with further detail of this pioneer College. It grew from strength to strength. The names of its Fellows form a constellation of such brilliancy as to be the envy and admiration of all—John Caius, Francis Glisson, William Harvey, Richard Lower, John Radcliffe, Robert Sibbald, Hans Sloane, Thomas Sydenham, Thomas Willis, Edward Wotton, and a host of others.

Whereas the Surgeons and Barber Surgeons undertook the teaching of their art after the manner of having apprentices, the Royal College of Physicians early began to give organized lectures and demonstrations, and consequently became the first center of medical education in the British Isles outside of the Universities. It will be remembered that William Harvey demonstrated and taught the circulation of the blood in his Lumleian lectures in 1616, twelve years before his first publication. All of those who obtained the privilege of the practice of Physic were not Fellows; the more junior branch were Members and could become Fellows only after a demonstration of their exceptional worth.

The physicians of Ireland and Scotland were not so fortunate as their London colleagues in obtaining early recognition. It was not until 1668 in Ireland, and 1681 in Scotland, that they obtained their Royal Charters. They were substantially framed upon the Royal College of London. They all threw their energies into teaching and granted after examination license to practise not only to those vouched for by themselves but graduates of Universities from the Continent and elsewhere. In fact, they were the

more progressive factors in medical education being rivalled by few of the Universities. This naturally stimulated the Companies and Guilds of Surgeons to put a better foot forward. For example, in Edinburgh the teaching of surgery had been at a rather slothful level until 1681 when the Royal Charter was given to the Physicians. They then bestirred themselves and put their house in order, and sought and obtained in 1694 what is stated to be the first authority in Scotland to carry out dissection and from such cadavers teach anatomy. The English surgical fraternities had moved much earlier but it is doubtful whether they taught anatomy except as a purely practical demonstration. They did not reveal any semblance of reaching the anatomical and physiological experimental accomplishments of the physicians during the seventeenth and eighteenth centuries. But still they slowly and surely progressed in organization until in 1784 the Royal College of Surgeons of Ireland, and in 1800 the Royal College of Surgeons of England, obtained their Charters as Colleges as distinct from Companies or Guilds. During the eighteenth century there is no doubt that all these Colleges and Guilds ably seconded the Royal College of Physicians of London in medical education. There were undoubtedly times when certain branches of teaching excelled in different centers,—for instance, the great Edinburgh School of Anatomy from approximately 1720 to 1830, or the London Surgeons of the latter part of the eighteenth century, and the Irish School of Physicians of the middle of the nineteenth century. But taking it all in all the physicians of the Colleges of London and Edinburgh left a lasting trail of high accomplishment until Simpson and Lister laid the foundations of modern technical surgery.

The point I want to make is that during four centuries these Royal Colleges of Physicians and Surgeons took a place not second to the Universities in medical education. They ranked equal to them in the certification or licensure of the medical practitioners and it was not until 1858 that the General Medical Council of Great Britain was created and invested with the sole power of assessing the " regular " and the " unregular " practitioner of medicine.

But did these Colleges do nothing else? Assuredly they did! They had an additional function which in our time has made them great and their Fellows honored and respected with cause. The certification of practitioners of Medicine and Surgery was not their sole function. They held out a higher ideal of accomplishment in the fact that to become a Fellow was a high distinction which was attained only after passing rigid examinations which gave evidence of superior accomplishments. As time passed, this naturally gave to them great power and also responsibility. In short, the bestowal of the hall-mark of the compleat physician or surgeon was the sole privilege of these Colleges and this they did by virtue of elevation to Fellowship of those they deemed worthy. So great was the faith in their award that it became the custom to require a certification of Fellowship in a Royal College of Physicians or Surgeons of all applicants to positions in hospitals

or teaching institutions of rank. This has been criticized as working hardship and favoritism on behalf of a relatively privileged few. The unfavorable but rare exceptions undoubtedly have occurred but these have accentuated the wisdom of the generally accepted rule. The Colleges have always been conscious of their responsibility and have erred, if anything, on the side of strictness for admission to Fellowship because of this trust.

The custom of having only Fellows of the Royal Colleges on the senior staff of the larger hospitals and on the faculty of teaching institutions dates back several centuries. The juniors may be Members of the Colleges of Physicians but Fellows only are eligible to the senior posts. This custom has operated to the benefit of the Colleges as well as the institutions. In the first place it required that the Colleges maintain a high level for their requirements. They have jealously guarded their reputation not only for professional ability but also for ethical standards. Institutions and the laity, on the other hand, have trusted their hall-mark to be worth always its face value and have seldom been disappointed. The Fellowship was a guarantee that the possessor had satisfied his peers that his training and knowledge of the specialty he professed were of such quality, and had been so tested by an impartial examination as to warrant them to bestow upon him this accolade of the elite. During the past 75 years this responsibility has become greater through the rapid progress of both medicine and surgery and the increasing need of broad and special knowledge.

But they have also through these centuries contributed other great boons to the medical profession. The physicians have developed their libraries and the surgeons their museums to the everlasting benefit of the profession. There has been, indeed, something of beautiful simplicity in their tacit acceptance of these responsibilities without carping rivalry but with sweet coöperation and help in each other's task.

What influence have these Colleges exerted on the rest of the English-speaking world? This question may be briefly dealt with under three headings. (1) For several centuries large numbers of young men from the Dominions and the United States flocked to them for both undergraduate and postgraduate training—the latter to aspire to a Fellowship and return, perchance, to their native lands with the accolade of their Order. (2) Their example influenced others to emulate them after a fashion. In North America there are the Colleges of Physicians and Surgeons of New York, Baltimore, of Ontario, of Quebec, and many others. But they have confined their activities almost entirely to undergraduate teaching or to the task of being more or less active Examining Boards for local licensure. There is, however, one College of Physicians in North America *par excellence* which I think I might specifically mention this evening with propriety—that of Philadelphia. There seems but little doubt that years ago some of the young men of this city after graduating from the Medical School of the College of Philadelphia went to Edinburgh and London to complete their studies, and were fired with the ambition

to found a College here. Dr. de Schweinitz reminds us that Samuel Powel Griffiths in 1783 expressly states that the idea of an American College of Physicians had several times occurred to him and three years later (1786) the College of Physicians of Philadelphia was founded. I have often wondered why the city claimed preference over the new Nation—probably the example of London and Edinburgh was the potent influence particularly as the Royal College of Physicians of London served as the prototype. Also, it must be remembered that it was not until 1800 that the Royal College of Surgeons of London received its Charter and in 1843 acquired the greater appellation of "England." The Constitution of the College of Physicians of Philadelphia has a nice familiar tone when compared with the Charter undoubtedly drawn up by Linacre over 250 years before—even to the four censors. Their careers have also been somewhat alike in their duties to their community and the perfection of their library. The difference, however, is clear cut and fundamental. Teaching in the broad sense and admission by examination have not been among the functions of the Philadelphian College. Undoubtedly conditions were different but for all that it created a medical aristocracy which for the greater influence was too exclusive.

(3) We now come to a third phase which has been born of a condition of affairs strangely similar in principles although not in detail with the conditions in the sixteenth and seventeenth centuries. Then the Corporation, Guilds and Colleges were formed to protect the public from "the multitude of ignorant persons"—"common artificers, as Smiths, Weavers and Women" who "boldly and accustomably take upon them great cures"; in other words, those who assumed knowledge which they did not have and imitated the honest practitioner of the day. By our State and Provincial Boards and other agencies we have imitated this function of the British Colleges, but only insofar as the general practitioner is concerned and not for those who profess to be specialists in Medicine and Surgery.

Here we arrive at the point where events indicate that such a College as ours appeared to be necessary. This necessity did not seem to have been a local need or confined to physicians or internists alone. Since 1913 five new Colleges in the English-speaking world, with aspirations more or less similar to the older order, have come into being,—The American College of Surgeons, The American College of Physicians, The Royal College of Physicians and Surgeons of Canada, The British College of Obstetricians and Gynaecologists, and The Royal Australasian College of Surgeons —five new, more or less exclusively elite, bodies in 22 years—one every 4 years. The whole range of the broader specialties of medical practice is represented. So now we come to our second question: Why was this spontaneous and widespread movement apparently necessary? Is medical practice in a somewhat similar position today to what it was four centuries ago in that those who are unqualified are presuming to invade the seats of the mighty? There seems little doubt that this is the answer. During

the past generation specialism in many branches of medicine has become rampant and has been professed by many who had no adequate preparation or right to do so and furthermore human nature has changed but little since the days of Henry VIII when it was deemed necessary to protect "most especially them that cannot discern the uncunning from the cunning." So, here we have the answer to our second question, namely, tc hall-mark those who have equipped themselves by special study and application to practise one or other of the senior branches of the medical art and science as distinct from those who have not so prepared themselves but would have the public believe that they have and so profess to all and sundry. To control such unwarranted assumptions has become the principal function of our elder sisters.

Are these younger Colleges trying to emulate the exclusiveness of their seniors in this matter? If so, it would be well to be thorough in the matter. Such a College or Society or Association must have certain standards for admission. But then all those that are reputable have. This now brings us to the difference between an association or a society and a college—not entirely the same significance it had in Roman law but what it has come to signify at the present day. I make bold to hold that it implies that it is only possible for one to enter the body of its membership after he has duly satisfied the appointed examiners or censors—call them what you please—by adequate and impartial tests of his worthiness. In a small or local community such tests are easy of application and so it was found by our older sisters, but as their fame spread and applicants presented themselves who were not known in person, or came from foreign countries or from lands across the seven seas, many of them near neighbors compared to our States and Provinces, the difficulties to enforce equality of standard became insurmountable without a uniform and impartial examination.

Gentlemen, we are at the parting of the ways. What other Colleges may do is their affair and none of our business, but what our future will be most certainly is our deep concern. Our Credential Committees have labored for years with an almost Herculean task—they have given of their best—but it is beyond human capacity to be arbiters of our membership from the information required and be satisfied that you have been fair and just to the College and the petitioners for membership. Are we to remain a rather select association and, as I have already said, an expensive one, or are we to be a College of Physicians to which its Fellows have been elected after passing such tests and examinations—moral, spiritual, and scientific—as to warrant the confidence of our people to trust him above those who are not, wheresoever he may go? That is the acid test! We as a College are responsible that it should be so and if we cannot command this we have failed in our self-appointed task, and our hall-mark of F. A. C. P. is of little worth. I do not wish to convey the impression that we have altogether failed, but I am thoroughly convinced that our methods

of assay must be improved until the world knows and has confidence in the products of our mint.

Now I am through! I thank you for your patience in enduring my rather domestic sermon but I have cogitated this matter for many years and believe that I am right and that history of the past supports me and that of the future will justify my belief.

In conclusion I want again to thank the College for bestowing upon me the highest honor that can come to an American Physician. To my colleagues, the Officers, the Board of Regents, and the Board of Governors, I wish to say an official and public farewell and thank them all for their unfailing support and courtesy during my tenure of office. I bid you all good luck and godspeed!

PRESENTATION OF THE JOHN PHILLIPS MEMORIAL MEDAL TO PROFESSOR LEO LOEB, OF WASHINGTON UNIVERSITY

Ladies and Gentlemen:

It is a custom of our College to award each year a medal in memory of our revered colleague, John Phillips. This medal is in token of notable contributions to the Science of Medicine. In awarding it this year your Board of Regents had in mind the rich accomplishments of a life-time devoted to researches in the Medical Sciences. During approximately forty years of active work Professor Loeb has contributed to many fields of general and experimental pathology. His first researches concerned the transplantation of pigmented skin which developed into a study of the main factors underlying transplantations in general and led to an analysis of organismal differentials and individuality in various life processes.

Early studies of wound healing led to investigations into the mechanism of growth, tissue culture and tissue formation in general and served as a model in the analysis of factors active in wound healing and inflammation.

His well known pioneer work on the transplantation of malignant tumors in animals made possible the study of heredity in tumors and the first quantitative determinations of this factor. Investigations concerning the relationship between hereditary factors and internal secretions in the origin of tumors led to a study of those of the ovary, the mechanism of the underlying sex cycle and to an analysis of certain hormones of the anterior pituitary and their significance for the ovary and the thyroid gland.

Since 1929 Professor Loeb has actively pursued his investigations of the action of the thyroid-stimulating hormone of the anterior hypophysis. In a long series of contributions on this subject, he has demonstrated in experimental animals increased mitotic activity of the thyroid cells, changes in the iodine content of the thyroid gland, elevation of oxygen consumption, accelerated circulation, exophthalmos and indeed most of the symptoms of Graves' disease.

Professor Loeb,—in recognition of these and many other notable contributions to Science, it gives me great pleasure and honor, on behalf of the American College of Physicians, to hand you this John Phillips Memorial Medal.

PHILLIPS MEMORIAL PRIZE ORATION

THE THYROID STIMULATING HORMONE OF THE ANTERIOR PITUITARY GLAND*

By Leo Loeb, *St. Louis, Missouri*

May I express to you, Mr. President and to the American College of Physicians, my deep appreciation of the honor you have conferred upon me. It is an interesting coincidence that you have invited me to discuss before you the thyroid stimulating hormone of the anterior pituitary gland here in Philadelphia, where about 30 years ago I began my investigations of the problems concerning internal secretions. At that time, I studied the functions of the corpus luteum and I found that one of its hormones sensitized the uterine mucosa so that when, subsequently, mechanical stimuli reached it, the maternal placentae or experimental placentomata were produced. In addition it could be shown that the corpus luteum prevents ovulation. These investigations in the course of time led to the study of the mechanism underlying the sexual cycle, which I have followed ever since. But about 16 years ago, I became also interested in the interrelations between various glands of internal secretion and I began to investigate the interactions between the thyroid gland and other glands with internal secretions, in particular the anterior pituitary. At first, I used in this work a commercial preparation of anterior pituitary gland, which evidently contained an admixture of thyroid substance and the latter predominated over the anterior pituitary substance proper. In the meantime biologists had made the interesting discovery that thyroid substance with its hormone is a necessary stimulant for metamorphosis in amphibia and that also anterior pituitary substance can exert a similar effect on metamorphosis provided the thyroid gland is present at the same time. The pituitary substance evidently acted by way of the thyroid gland; it stimulated the latter to function, as the studies of Allen, P. E. Smith, Uhlenhuth, Spraul, Hogben and Hoskins have shown; and Uhlenhuth in particular noticed, during this process, indications of an enlargement of the thyroid acini and of an increased secretion of the acinus cells. This effect of the thyroid on amphibian metamorphosis was subsequently introduced, as a test for the presence of thyroid hormone, into experimental pathology and clinical medicine and proved of value—an example of fruitful coöperation between pure biology and clinical medicine. It was also shown by P. E. Smith and Foster that extirpation of the anterior pituitary in rats led to an atrophy of the thyroid gland.

About seven years ago, we began a reinvestigation of the relation be-

* Read at the Philadelphia meeting of the American College of Physicians, May 1, 1935.
Department of Pathology, Washington University School of Medicine, St. Louis, Mo.

tween anterior pituitary and thyroid gland, but this time we used our own anterior pituitary preparation and, as in our previous investigations, it was the guinea pig which served as test animal. Very soon it was found that after a few injections of this anterior pituitary extract, which was obtained from cattle, the whole appearance of the thyroid gland changed radically. The colloid softened and was absorbed, the acinus cells became high cuboidal and cylindrical. The acini changed their shape. Instead of round acini, lined with rather low cuboidal cells, there developed longitudinal, often curved, winding slits lined with high cylindrical cells. It was difficult to identify in the microscopic picture the gland thus produced with the thyroid, and yet it closely resembled the thyroid gland as found in very pronounced cases of Graves' disease or exophthalmic goiter, where nature has apparently made a similar experiment. Moreover, we observed that, during the period of injections of anterior pituitary extracts, the animals lost weight. This suggested the possibility that through longer continued injections the other principal symptoms of Graves' disease might also be imitated. With the coöperation of our associates—and soon others also began to take part in this work—this possibility was realized. It is an interesting experience to follow how step by step the symptom-complex of Graves' disease was reproduced in the guinea pig. In addition to the structural changes in the thyroid gland itself similar to those characteristic of severe cases of this disease and to the loss in body weight, the basal metabolism rose considerably; the eyes of the animal began to protrude; tachycardia and nervousness, as indicated by an intensified reflex activity, became manifest. The glycogen in liver and muscle was mobilized and the adrenal cortex showed considerable increase in cell divisions. The stimulation of the thyroid gland led to solution processes in the colloid and thus to a constant discharge of an increased amount of organic iodine into the blood stream. Therefore the blood became richer in these organic iodine compounds, among which thyroxin is especially important.

In this connection it may be of interest to refer briefly also to the action of inorganic iodine on the thyroid gland. Under ordinary conditions this kind of iodine stimulates the thyroid gland. But if inorganic iodine is given concomitantly with anterior pituitary hormone, it inhibits the latter in its stimulating action on the thyroid gland and thus it resembles thyroid hormone which invariably inhibits the functioning of this organ. Now, it is well known, especially through the observations of Plummer, that also in exophthalmic goiter iodine at least temporarily reduces the activity of the thyroid gland and makes an operative removal of this organ possible in otherwise unfavorable cases. We notice then an almost complete correspondence between the effects of the injections of extracts of anterior pituitary of cattle into guinea pigs and the symptom complex of Graves' disease.

There still remains to be considered the correlation between the stimulation of the thyroid gland and the changes which take place in the ovary

under the influence of the hormones of the anterior pituitary. If we inject acid extract of cattle anterior pituitary into female guinea pigs, we notice a destructive effect exerted by this substance on the ovarian follicles, which undergo an early retrogression (atresia). At the same time, the theca interna may manifest a slight degree of luteinization in certain atretic follicles and occasionally a large follicle may become converted into a pseudocorpus luteum. Similar is the effect of the extract of anterior pituitary of hog and sheep. The implantation of the glands from these species acts in a corresponding manner to the injection of extract, although the effects of the injections are slightly more pronounced. If we implant one or two guinea pig anterior pituitaries, noticeable hypertrophy of the thyroid is usually lacking; there is induced merely the formation of very large ovarian follicles, the granulosa of which matures, and of some strands of interstitial gland in the medulla of the ovary. But if we implant several guinea pig anterior pituitaries into a female guinea pig, the effects may become more intense in the ovary and at the same time a slight hypertrophy may appear also in the thyroid gland. Anterior pituitaries of rat, of rabbit and of man cause marked luteinization of the granulosa, as well as of the theca interna, and these processes are accompanied by a noticeable hypertrophy of the thyroid gland, but the different species may again show certain minor variations among themselves. We see then that the experimentally produced hypertrophic changes in the thyroid gland, as a rule, are associated with definite changes in the ovary of the guinea pig; it does not therefore seem advisable to us at present to apply to the thyroid stimulating hormone the term thyrotropic, in the sense that the action of this hormone is limited to the thyroid gland. We further notice that the effects of the anterior pituitary glands from different species are in certain respects specific.

In regard to the various changes induced by introduction of anterior pituitary gland some of these are the result of the stimulation of the thyroid gland and may therefore be considered as indirect changes. This applies especially to the effects on metabolism, heart rate, reflex action and presumably on carbohydrate metabolism, but it does not apply to the effects on the ovary; the destructive action which cattle anterior pituitary exerts on the ovarian follicles is not caused directly by thyroid hormone, as experiments in thyroidectomized guinea pigs indicate. On the contrary, the thyroid hormone itself seems to cause an increased growth of the ovarian follicles. It is also probable that the effects on the eye and on the adrenal gland do not take place by way of the thyroid gland.

If we may then be able to state that, by inducing experimentally an increased activity of the anterior pituitary gland in the guinea pig, it is possible to reproduce the essential symptoms of Graves' disease in man, this does not necessarily mean that increased activity of this gland is the essential factor underlying Graves' disease, but it suggests, at least very strongly, that in some way the anterior pituitary is involved in this condition. However, there is apparently one serious objection to such a con-

clusion, namely the fact, observed by us several years ago and since confirmed by Collip and Anderson and others, that if we continue the injections of anterior pituitary extract for a long period of time, the thyroid gland as well as the sex organs step by step return to their normal state. On the other hand, we know that Graves' disease is not as a rule a self-limiting disease, although remissions may take place. When we first made this observation concerning the establishment of an active resistance to injections of anterior pituitary extracts, we pointed out the possible significance of this occurrence as an explanation of remissions in Graves' disease. It is possible that, after a cessation of the administration of the extract continued over a longer time, injections might again become effective, and the resistance thus established might in reality correspond to a remission.

As to the mechanism underlying this acquired resistance, we found in our first experiments that the blood serum of the resistant animals does not exert a direct neutralizing action on the hormone. More recently Collip and Anderson have made the important discovery that through injection of such serum it is possible to induce in the injected animal reactions, of an as yet unknown nature, which somehow counteract the effects of the hormone, at least for a certain period.

It is, however, conceivable that other mechanisms, which have been shown to function in the development of resistance and which exert their influence primarily by acting on tissues and organs in a specific manner, may secondarily cause the entrance into the circulation of substances which inhibit the response of tissues to the stimulating action of anterior pituitary hormone. We were able to demonstrate that as stated iodides, as well as thyroid hormone, inhibit the effect of the anterior pituitary hormone on the thyroid gland, largely in all probability by diminishing the responsiveness of the thyroid gland to this hormone. Thus a self limiting mechanism can be shown to exist. Anterior pituitary hormone stimulates the thyroid gland; following this stimulation, thyroid hormone is given off in increased amounts into the circulation and the latter substance then counteracts the effect of the anterior pituitary hormone. But there is a second self regulatory mechanism, which likewise tends to limit thyroid activity. As a result of the secretion of thyroid hormone, the basal metabolism is increased and this increase usually leads to a loss in weight of the individual thus affected. Now, in experiments with guinea pigs, a loss in body weight in itself tends to cause a return of the thyroid gland to a resting state. The acinar epithelium becomes low, the acini small and the colloid hard. Under such conditions the amount of thyroid hormone given off into the circulation would be reduced and the effect of the thyroid stimulating hormone would be limited. There are in addition indications that still other mechanisms of a cellular nature may exist which tend to regulate and restrict thyroid activity; this follows from the rapidity with which the multiplication of acinar cells in the stimulated thyroid gland begins to decline, notwithstanding the continued application of the stimulus.

It has recently been suggested by Kuschinsky, as well as by Loeser and Thompson, that the stimulating action, which iodine exerts on the thyroid gland, as well as the inhibiting action of thyroid hormone, is mediated by the anterior pituitary gland. While it seems probable that the anterior pituitary gland is indeed concerned in such effects, still there are reasons for the conclusion that these substances act also directly on the thyroid gland.

There is another consideration which has some bearing on the question with which we are here primarily concerned, namely the significance of the anterior pituitary gland in the etiology of exophthalmic goiter. Clinical observation points to the importance of an inner constitutional factor, supplementary to the stimulating factor, in the origin of this disease, as is the case in so many other diseases. This constitutional factor may modify the response of the organism to the stimulating factor, and thus prevent the full effect of mechanisms which otherwise might tend to counteract the hormone action in normal individuals.

Considering the preponderating influence, which the anterior pituitary gland, by way of its hormone, exerts on the thyroid gland, on the growth of the latter and on its metabolic activity—two functions which as a rule seem to go hand in hand—as well as the fact that all the principal symptoms of Graves' disease can be reproduced by administration of the thyroid stimulating hormone of the anterior pituitary gland, there seems to be some justification for the belief that the action of the anterior pituitary is involved in the etiology of Graves' disease, although it may be only one of several factors concerned in this condition. However, though the experimental reproduction of a disease complex may make it very probable that the disease itself originates in a similar manner, still it does not afford conclusive proof. While it may be difficult to furnish such a conclusive proof, several lines of investigation suggest themselves, and we have recently undertaken experiments which, we hope, may lead to a more direct answer to this problem. One of the difficulties which we have to face at present is the lack of definite knowledge as to the number and kind of hormones which are produced in the anterior pituitary gland. So far, we merely know the effects initiated by substances given off by this organ and acting as hormones. However, quite recently with the coöperation of our associates, we have found a method which permits us experimentally to suppress at will certain activities of the anterior pituitary gland, while enhancing others, and to transform the action of the anterior pituitary gland, which is characteristic of one species, into that of a different species.

These recent investigations which are not yet finished, seem to confirm tentative conclusions which we had drawn on the basis of previous observations, namely that as far as the action of the anterior pituitary gland on the ovary is concerned we may distinguish in the main two substances, namely a follicle-stimulating hormone, which also induces maturation processes in the follicles, and a second substance inducing atresia which means destruction of follicles. The latter action may be associated with a very

moderate formation of pseudolutein and interstitial gland tissue. This effect may perhaps be due to a third substance. It can be shown experimentally that the anterior pituitary glands of different species differ as to the relative preponderance of these substances. The possibility of separating thus these substances acting on the ovary and the associated thyroid stimulating hormone by experimental chemical means, may, we hope, open the way for approaching in a more direct manner the problem as to the significance of the anterior pituitary gland in the etiology of Graves' disease.

Let me say in conclusion that I am fully aware of the incompleteness of these investigations at the present time, and also of the fact that whatever has been accomplished is due to the coöperation of my associates and of other investigators. But may I also be permitted to point out that these investigations very well exemplify the advantages which accrue to clinical medicine from coöperation with biology, physiology and experimental pathology. They all should be encouraged to proceed in their own way and to seek their own problems. At some point they will meet for fruitful association. They are not sharply separable and essentially they form one connected whole. While the cure of disease is the direct aim of clinical medicine, the analysis of man and life, in relation to the environmental factors operating in the universe, at which biology aims, will help the physician to approach, with a broader understanding and deeper sympathy, the problems which his patient faces, in a world to which after all our body and mind are not fully adapted.

THE PRESENT STATUS OF ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF LOBAR PNEUMONIA *

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THERAPEUTIC innovations begin with an original idea or more often with a new application of an old one and, if promising and spectacular, may be followed by premature and unjustified optimism. After experimentation and thorough clinical trial have established their status, they are either accepted or rejected.

In connection with the therapeutic use of pneumothorax in pneumonia we have passed through a period of enthusiasm which was initiated primarily by empirical use of the method; and only later obtained the confirmation of experimental evidence. That this order was the reverse of what it should have been is beside the point.

The past year has been devoted to further animal experimentation and more thorough clinical trial and, although insufficient time has elapsed to warrant final judgment, enough information is available to permit the expression of certain opinions derived from a critical analysis of the data. We are concerned with the reports on 197 cases of lobar pneumonia which have either appeared in print or have been submitted to the authors prior to publication. This latter courtesy is herewith gratefully acknowledged.

The following table lists the names of authors, the number of cases in each report, and the mortality rates.

It is an accepted fact that the mortality of lobar pneumonia in general

TABLE I

Number of Cases and Mortality of Lobar Pneumonia Treated by Artificial Pneumothorax (American authors March 1934 to April 1935)

Authors	No. of Cases	Died	% Mortality
Blake, Howard and Hull [1,2]	43	11	25.5
Robertson, Behrend, Cowper and Tuck [3,4,5]	51	20	39.2
Stoll [6]	29	7	24.1
Leopold and Lieberman [7]	16	5	32.0
Moorman [8,9]	10	3	30.0
Isaacs, Udesky, de Pinto [10]	7	4	57.1
Hammond [11]	7	1	14.3
Crowell [12]	4	1	25.0
Hines and Bennett [13]	12	4	33.3
Holmes and Randolph [14]	18	2	11.1
Totals	197	58	29.4

*Read at the Philadelphia meeting of the American College of Physicians, April 30, 1935.

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hospitals throughout this country ranges between 25 and 35 per cent Therefore, it would appear that therapeutic pneumothorax has been neither helpful nor harmful and has had no influence on the death rate of this disease. This statement is true and will continue to be true if this treatment is used as indiscriminately in the future as it has been in the past.

The mortality from lobar pneumonia under any form of treatment, specific or non-specific, is conspicuously influenced by age, type of pneumococcic infection, bacteremia, spread, and postpneumonic complications. The results of specific serum therapy depend largely on the day of the disease on which such treatment is instituted. Early treatment is even more important when artificial pneumothorax is used.

In addition to the above named factors, there is one more which may be disregarded under the usual methods of treatment but which is of fundamental importance in compression therapy. Preëxisting fibrous pleural adhesions render this type of treatment inadequate or useless. Recent pleural adhesions, developing as the result of the extension of the acute infectious process from the lung to the adjacent pleura, may have a similar effect.

Let us proceed to analyze the cases treated by artificial pneumothorax in relation to those factors which most significantly influence mortality. This task is made difficult in many cases by the multiplicity of determining factors, such as the coexistence of bacteremia and spread.

Age. After infancy, and during childhood, lobar pneumonia is a comparatively innocuous disease with a mortality of 3 or 4 per cent. The incidence of empyema in infancy and childhood is 12 per cent. It is apparent from a survey of the cases in infancy and childhood treated by artificial pneumothorax that there is greater likelihood in them of spontaneous pneumothorax and empyema. We do not believe that this method of treatment should be employed in this group and we can see no possible justification for its use in the treatment of late post-pneumonic complications as practiced by several continental writers.[15, 16, 17, 18]

At the other extreme of life the greater probability of chronic adhesions and the increased prevalence of Type III infection which may produce a plastic exudate interferes with but does not contraindicate compression therapy.

Day of Disease. It is apparent that too few authors have been sufficiently impressed by the fundamental importance of early treatment and many cases have been treated too late. Most of these should not have had therapeutic pneumothorax. Blake's complete statistics which have been placed most generously at the writer's disposal prior to their publication are most instructive. He treated one case on the first day, seven on the second and 17 on the third. Of these 25 cases, one died—with bacteremia and contralateral spread. Twenty-four recovered. Sixteen were treated on the fourth day and two on the fifth. Of these 18 cases 10 died.

This is tremendously significant in view of the fact that the average age of the recovered cases was 33.5 years while the average age of the fatal

cases was 43 years—a difference which cannot possibly explain a mortality of 4 per cent in those treated within the first three days compared to a mortality of 55.5 per cent in those treated on the fourth and fifth days.

Bacteremia. The incidence of bacteremia and its attendant mortality in 128 treated adult cases is shown in table 2.

TABLE II

Incidence of Bacteremia and Mortality in 128 Adult Cases of Lobar Pneumonia Treated by Artificial Pneumothorax

Authors	No. of Cases	Died	Bacteremia	Died
Blake, Howard and Hull	43	11	12	7
Stoll	29	7	5	5
Leopold and Lieberman	16	5	5	1
Behrend, Tuck and Robertson	40	14	5	4
Totals	128	37	27	17

The incidence of bacteremia was 21 per cent and its mortality was 63 per cent. From this small series of cases, no deductions can be drawn regarding the effect of artificial pneumothorax on bacteremia except to say that it is of no apparent value when first employed after blood stream invasion has occurred. Much more experimental work must be undertaken and many more patients will have to be treated early and effectively before any conclusions can be drawn in regard to the value of compression therapy in preventing blood stream invasion.

Spread. The incidence of spread, determined clinically, in lobar pneumonia is about 10 per cent, at necropsy 16 per cent. The mortality is almost doubled when two or three lobes on the same side are involved and is nearly tripled when both lungs are implicated. The following table shows the incidence and mortality of spread in 86 treated cases.

TABLE III

Incidence of Spread and Mortality in 86 Adult Cases of Lobar Pneumonia Treated by Artificial Pneumothorax

Author	No. of Cases (Early)	Spread	Died	No. of Cases (Late)	Spread	Died
Leopold and Lieberman	11	3	3	5	2	1
Blake, Howard and Hull	25	3	1	18	8	6
Isaacs, Udesky and de Pinto	4	1	1	3	2	2
Hines and Bennett	2	1	1	10	1	1
Holmes and Randolph	3	0	0	5	0	0
Totals	45	8	6	41	13	10

The total incidence of spread in these 86 cases was 24 per cent, more than twice that found by clinical examination under all other methods of treatment. Spread occurred in 17 per cent of cases treated early and in 31 per cent of those treated on the fourth day or later. In this connection it is of interest that contralateral spread did not occur in a single one of our treated

experimental animals, all of which received pneumothorax within the first 48 hours.[19] The mortality from spread in these 86 cases was 76 per cent.

It would appear that compression therapy in the first three days neither retards nor provokes extension to the opposite side. Again, many more cases must be treated early and adequately before this opinion can be either confirmed or disproved.

We believe that unsuccessful attempts to compress the involved lobe or lung, on or after the fourth day, increase the danger of contralateral spread. If this is true, therapeutic pneumothorax is contraindicated after the first 72 hours of lobar pneumonia.

Complications. Empyema occurs in about 3 per cent of cases of lobar pneumonia in adults. It was present in nine of the 180 adults in the pneumothorax treated group, an incidence of 5 per cent. Five of these were in Blake's series. His incidence was 11 per cent. Blake attempts to get complete collapse as rapidly as possible, sometimes injecting as much as two liters of air at the first treatment. It appears that artificial pneumothorax does not increase the likelihood of empyema unless positive pressure is deliberately produced and maintained.

In this entire pneumothorax group, 17 children were treated, three by Moorman, with empyema in one and spontaneous pneumothorax in another, four by Crowell with no such complications, and 10 by Holmes and Randolph with four empyemas, three of which were accompanied by and may have resulted from spontaneous pneumothorax. Holmes and Randolph's two fatal cases had empyema. In each the pleural cavity was so adherent that only a small amount of air was injected under positive pressure. In retrospect, the authors state that neither of these cases should have been treated.

The favorable prognosis of lobar pneumonia in childhood and the increased risks of serious complications from compression therapy would seem to argue against its use in this group.

Adhesions. There are only two ways to find pleural adhesions in the living pneumonia patient. Their presence may be inferred from the production of positive pressure and pain during instillation of air and they may be demonstrated by roentgen-ray after such injections. *An amount of air more than sufficient to completely compress a pneumonic lung may be injected easily, without positive pressure and without pleural pain, and yet roentgen-ray may demonstrate adhesions which altogether prevent effective compression.* Preëxisting fibrous adhesions are the greatest obstacle to early effective pneumothorax therapy. If this is true, it is obvious that the mathematical probability of their presence should be determined, if this is possible.

Through the courtesy of Dr. Krumbhaar and the Department of Pathology, records of patients autopsied at the University Hospital were placed at our disposal. Consecutive protocols were examined, discarding all those which revealed any type of acute or chronic pulmonary disease except ter-

minal bronchopneumonia. The results of this survey are presented in the following table:

TABLE IV

Incidence of Fibrous Pleural Adhesions in 515 Consecutive Autopsies (Acute and Chronic Pulmonary Disease Omitted Except Terminal Bronchopneumonia)

Age Group	Number of Cases	Old Adhesions	% Old Adhesions
10–19	43	10	23.3
20–29	64	29	45.3
30–39	70	26	37.1
40–49	87	42	48.3
50–59	108	55	50.9
60–69	93	55	59.1
70–79	45	23	51.1
80–89	5	2	40.0
Total	515	242	47.0

Separating the cases into decades it is apparent that from 10 to 20 years of age, old pleural adhesions are found post mortem in approximately 25 per cent of individuals dying from various causes exclusive of pulmonary disease. After the age of 20 they are present in about 50 per cent of all such cases.

How does this table tally with the presence of adhesions noted by those who have treated pneumonia by pneumothorax and tabulated this finding? Our incidence was 62 per cent, Blake's was 56 per cent, that of Holmes and Randolph 55 per cent.

Seeking an explanation for the extraordinary difference in mortality between Blake's cases treated before the end of the third day and after this time, we studied 55 autopsy records of patients dying of lobar pneumonia, paying particular attention to the type of infection, the day of death, and the pathologic changes in the pleura. While the information obtained is not sufficiently clear-cut to lend itself to statistical tabulation, the findings are of great interest. Thirty-eight per cent of these cases (irrespective of age) showed old adhesions. In addition to this, it was noted in the protocols that many of the patients dying early in the disease had fibrinous or serofibrinous pleurisy over the adjacent affected lobe or lobes, while many of those dying late showed fibrous pleurisy and in some there was a plastic exudate partially obliterating the pleural cavity. This was particularly true in Type III infection.

Reverting to Blake's tables which record the day on which the temperature first returned to normal, in those who recovered without complications, it is found that an artificial crisis was produced most frequently in the cases treated early. None of the patients treated after the third day had a normal temperature until several additional days had elapsed. In other words, it seems probable that during the third day, and much more frequently thereafter, recent adhesions prevent adequate compression and artificial crisis.

We firmly believe that the involved lobe or lung must be completely surrounded with air if artificial crisis is to be achieved and this can only occur

if the pleural cavity is almost entirely free. Unless this treatment can provoke an artificial crisis it does no good and the patient goes on to crisis or lysis at the expected time. Termination by crisis is no proof of efficacy of treatment unless the crisis is artificially induced by it. In those treated early, where the pleural cavity is free, the effect is dramatic.

Summary and Conclusions

The records of 197 cases of lobar pneumonia treated by artificial pneumothorax are reviewed. The death rate in this group is essentially the same as general hospital mortality from this disease under all other forms of treatment. We have not attempted to revise our statistics by excluding the palpably hopeless because no distinctions are drawn in compiling hospital mortality.

For the reasons which we have given, we disapprove of the use of artificial pneumothorax in lobar pneumonia in children.

This treatment is probably without effect on preëxisting blood stream invasion but may possibly prevent late bacteremia if it is used effectively before blood stream invasion occurs.

It is probable that early treatment neither increases nor decreases the usual incidence of spread. There are good reasons to believe that late treatment increases the chances of its occurrence. If this proves to be correct, artificial pneumothorax is contraindicated in lobar pneumonia after the third day of this disease.

It does not increase the incidence of empyema in adults unless such large quantities of air are introduced that positive pressures are deliberately produced and maintained.

The greatest obstacle to effective early treatment is the presence of preexisting fibrous adhesions in almost 50 per cent of adults of middle age. This barrier is almost insurmountable in patients treated after the third day because the pleural reaction after this time adds new adhesions to the predictable 50 per cent already present, thus making complete compression and artificial crisis virtually impossible.

Artificial crisis can only occur with a free pleural cavity, band adhesions possibly excluded, and may be expected in 50 per cent of cases treated before the fourth day. This statement is predictable and is in accord with clinical experience. Nothing is accomplished by compression treatment unless artificial crisis is achieved.

Specific serum therapy is applicable to about 50 per cent of all patients with lobar pneumonia. Artificial pneumothorax is capable of producing an artificial crisis in about the same proportion of cases and can be used in any and all types of lobar pneumonia provided the involvement is unilateral. Both specific serum and pneumothorax must be used early to be effective. Artificial pneumothorax properly used is a real and permanent addition to the treatment of lobar pneumonia. In those cases in which artificial crisis is induced, one is privileged to witness an apparent miracle.

There is never any contraindication to any other type of treatment, specific or non-specific, and the most favorable results will be achieved by the rational and coincident use of all appropriate therapeutic measures.

BIBLIOGRAPHY

1. Blake, F. G., Howard, M. E., and Hull, W. S.: The treatment of lobar pneumonia by artificial pneumothorax, Trans. Assoc. Am. Phys., 1934, xlix, 119–137.
2. Blake, F. G.: Personal Communication.
3. Behrend, A., and Cowper, R.: Artificial pneumothorax in the treatment of lobar pneumonia, Jr. Am. Med. Assoc., 1934, cii, 1907–1913.
4. Behrend, A., Tuck, V. L., and Robertson, W. E.: Artificial pneumothorax in the treatment of lobar pneumonia, Jr. Lab. and Clin. Med. (In press.)
5. Robertson, W. E.: Personal Communication.
6. Stoll, H. F.: Personal Communication.
7. Leopold, S. S., and Lieberman, L. M.: The treatment of lobar pneumonia by artificial pneumothorax, Med. Clin. N. Am. (To be published.)
8. Moorman, L. J.: Artificial pneumothorax in treatment of pneumonia, South. Med. Jr., 1934, xxvii, 233–237.
9. Moorman, L. J.: Artificial pneumothorax in the treatment of pneumonia—report of cases, Internat. Clin., 1934, iv, 119–131.
10. Isaacs, H. J., Udesky, I. C., and De Pinto, A.: Pneumothorax treatment of lobar pneumonia, Illinois Med. Jr., 1934, lxvi, 267–270.
11. Hammond, J. J.: Personal Communication.
12. Crowell, L. A., Jr.: Pneumothorax treatment in lobar pneumonia, South. Med. and Surg., 1934, xcvi, 467–470.
13. Hines, L. E., and Bennett, D.: Artificial pneumothorax in the treatment of lobar pneumonia, Arch. Int. Med., 1935, lv, 100–111.
14. Holmes, F. G., and Randolph, H.: Treatment of lobar pneumonia by artificial pneumothorax, Ann. Int. Med., 1935, viii, 1008–1027.
15. David, O.: Zur Pneumothoraxbehandlung der Lungenentzündung, Deutsch. med. Wchnschr., 1921, xlvii, 802.
16. Ibrahim, J., and Duken, J.: Zur Behandlung der kindlichen Pneumonie mit dem künstlichen Pneumothorax, Arch. f. Kinderh., 1928, lxxxiv, 241–249.
17. Duken, J.: Die künstliche Pneumothorax in der Behandlung der kindlichen Pneumonie, Klin. Wchnschr., 1930, ii, 2195–2199.
18. Jahr, J., and Neumann, R.: Zur Pneumothorax-Behandlung der Säuglingspneumonie, Klin. Wchnschr., 1930, ix, 2200–2202.
19. Lieberman, L. M., and Leopold, S. S.: Therapeutic pneumothorax in experimental lobar pneumonia in dogs, Am. Jr. Med. Sci., 1934, clxxxvii, 315–330.

AGRANULOCYTOSIS *

By Henry Jackson, Jr., M.D., *Boston, Massachusetts*

It would be impossible adequately to cover all aspects of the disease agranulocytosis in the time at my disposal. I have chosen, therefore, to attempt to clarify, in so far as my knowledge of the subject permits, certain phases of the condition which are at present under dispute. Brevity necessitates a certain amount of dogmatism for which I have but little enthusiasm.

In the first place, is there such a disease entity at all? I believe there is. It is characterized by extreme leukopenia and neutropenia and occurs at all ages except early childhood. The onset is usually sudden, fever is constant and in the majority of instances ulcerative or even gangrenous lesions appear in the oral cavity, gastrointestinal tract and elsewhere. The disease runs, as a rule, a rapid course, ending in recovery or death in a short time. Much more rarely the disease is subacute or regularly recurrent. In the true condition there should be no anemia of moment, unless due to some unrelated disease, no thrombopenia, no hemorrhages into the skin or mucous membranes and the blood smear should show few, if any, immature white blood cells. There should be no lymphadenopathy not readily accounted for by adjacent sepsis nor any notable enlargement of the spleen. Unless these criteria are adhered to with some semblance of strictness, hopeless confusion results, as can readily be seen by perusal of the literature, particularly the French.

Yet leukopenia in and by itself does not make the diagnosis. I cannot emphasize this point too strongly. Leukopenia and neutropenia are common to many diseases—pancytopenia, pernicious anemia, benzol poisoning, arsenic poisoning, Kala-azar, miliary tuberculosis and certain instances of acute aleukemic leukemia. Each of these diseases has clinical and hematological characteristics which serve in most instances to identify it. Before the diagnosis of agranulocytosis is decided upon one must carefully eliminate all these. There remains what for lack of a better term may be called agranulocytosis. Mettier estimated that but 6 per cent of all leukopenias in his clinic could properly be called agranulocytosis. Doan has reached similar conclusions.

The pathological changes in the bone marrow in agranulocytosis have been so diversely described that one is left utterly bewildered and this state of affairs has served as an opening wedge for those who maintain that agranulocytosis is not a true disease, but merely a symptom complex. It is fortunate, therefore, that Krumbhaar and Fitz-Hugh and more recently Custer of Philadelphia have come forward with a clear cut and masterly description of the changes found in the true disease. From an analysis of 11 cases coming to postmortem Custer concluded that there was a marked

* Read at the Philadelphia meeting of the American College of Physicians, May 3, 1935.

proliferation of the myeloblasts with a failure of these cells to mature, a view first suggested by Fitz-Hugh and Krumbhaar. The other elements of the bone marrow were undisturbed. More or less hyperplasia of the femoral marrow occurred, especially in the more chronic cases. From an analysis of 27 cases of my own coming to autopsy I have reached essentially the same conclusions and I heartily agree with Custer that the bone marrow of agranulocytosis secondary to arsenical poisoning is quite different. Certainly the bone marrow of true agranulocytosis bears no resemblance to that of pernicious anemia, aplastic anemia, or acute leukemia —all diseases which may give extreme leukopenia. Yet without examination of the bone marrow one may be unable to diagnose which of these conditions obtains.

We have then a characteristic clinical picture with a correspondingly characteristic pathological one. Such would appear to justify the cataloguing of agranulocytosis as an entity, at least until we are able to speak in terms of physiological pathology.

What then of the etiology of agranulocytosis? A few years ago there was hardly a speculation as to the cause of the disease. Now the pendulum has swung the other way and it is the fashion to incriminate amidopyrine as the most common, if not the sole, cause. There is unquestionably considerable evidence that amidopyrine may be, in at least certain cases, of etiological importance, but the *post hoc ergo propter hoc* argument is notoriously fallacious and I believe it behooves us to be cautious before drawing too broad conclusions. There is no question but that many cases of agranulocytosis follow long or massive administration of the drug. I have seen many such. But some of these very same cases recover in spite of increased administration of the same drug during the height of the illness. The drug cannot both cause and cure the disease. Furthermore, I have many instances in which there was no evidence whatever that any such drug had been taken prior to the attack. Again there are patients who have taken amidopyrine and become ill with the disease, stopped the drug completely and still had one or more relapses; and finally I have seen instances in which the attack has been apparently precipitated by amidopyrine, increased dosage of which after complete recovery has produced not the slightest change in the blood picture. It has been suggested that agranulocytosis has virtually disappeared and that this disappearance is due to the withdrawal of the drug from the market. Yet the evidence is that the sales of amidopyrine in this country were greater in the last six months of 1934 than ever before. I hold no brief for the harmlessness of amidopyrine but I must point out what I believe to be a fact—that amidopyrine has not been proved to be the sole or even the major cause of the disease. That it is of importance in certain cases I do not for a moment deny.

That an endocrine factor may be at the basis of some cases is suggested by those instances in which the onset occurs at the time of menstruation

but I know of no work which has disclosed experimentally the nature of this endocrine abnormality.

Personally I am inclined to believe that the disease agranulocytosis is of varied etiology, but there would seem to be no good reason for denying the existence of the entity on this ground alone. Pernicious anemia may be due to lack of an intrinsic factor, to radical surgical interference with the gastrointestinal tract or to malignant disease preventing the proper functioning of such factors as cause a proper maturation of the red cells. In a similar manner a variety of agents, known and unknown, may prevent proper maturation of the granular white cells and so produce the disease agranulocytosis.

Now as to the treatment of the disease. I enter this phase of the discussion with many misgivings, for it has been my lot to be responsible for one form of treatment. Certain forms of therapy, such as sterile milk, leukocytic extract and the like can be disposed of as valueless. Roentgen-ray is probably useless. When one comes to transfusions, there is less unanimity of opinion. Unquestionably cures have followed transfusion, as they have occurred spontaneously and following a large variety of remedies, but there would not seem to be convincing evidence that they are actually beneficial, and numerous authors have pointed out that following them the white count may fall even to lower levels. Personally I am decidedly against transfusions in this disease.

Pentnucleotide was introduced in 1929 and has been used with varying success by a large number of physicians all over the world. Curiously enough it would appear that in the hands of some there were rather uniformly good results, while others have had consistently poor results. The explanation of this apparent fact is not clear. Granting for the moment the premise that pentnucleotide is of value in the treatment of agranulocytosis, it is well to inquire as to the cause of such failures as have been recorded. There would seem to be two important factors. One is dosage. Again and again in the literature one finds case reports indicating that pentnucleotide was of no avail, yet careful analysis of the cases shows that but a half or a quarter or even less than the recommended amount was given. Such reports do not militate against the possible usefulness of the drug. It is generally agreed that liver extract will cure pernicious anemia, but it must be given in sufficient amounts to be effective. We recommend now that 40 c.c. pentnucleotide be given each day intramuscularly. One cannot judge its effectiveness, or lack of it, from smaller amounts. Unfortunately in certain instances fairly severe systemic reactions occur, so it is well to start with smaller amounts before proceeding to the larger, and in some instances full amounts cannot be given at all. It is useless, however, to give small infrequent amounts.

Further, it must be recognized that agranulocytosis is often a fulminating disease and that complete absence of granulocytes for more than a relatively short time is probably incompatible with life. In spite of adequate

dosage of a theoretically potent drug, therefore, a patient may die before the beneficial results accrue.

The second factor in the apparent failure of pentnucleotide in certain cases would appear to be improper diagnosis. As Custer says, the diagnosis of agranulocytosis can often be negated by a glance over the clinical records. There has never been any claim that pentnucleotide will cure acute leukemia —even in the aleukemic stage—yet the clinical differential diagnosis between aleukemic leukemia and agranulocytosis may be fraught with the greatest difficulty. There has never been any claim that pentnucleotide will cure aplastic anemia or pernicious anemia, yet many times, particularly in the foreign literature, instances of accompanying leukopenia in these diseases have been labelled agranulocytosis and treated as such. Again I would emphasize that leukopenia in and by itself is no criterion for the diagnosis of agranulocytosis. If we grant the existence of a disease entity we must confine our therapeutic aims to this entity before deciding on their merits.

Liver extract has recently been suggested as a cure for agranulocytosis. There is no question that cures have followed its use, but if such sequence of events be regarded as evidence of the effectiveness of the drug in this disease, how many more data have we on this score alone? Furthermore, many of the cases reported as cured by liver extract are obviously pernicious anemia with extreme leukopenia. Of this there can be no doubt. Bonsdorff treated two cases with liver intravenously with recovery in both instances. There seems to be no reason to doubt, however, that the first patient was suffering from pernicious anemia. She had a red blood cell count of 528,000 per cu. mm., a color index of 1.32 and a white count of 1,750. His second patient had extreme leukopenia apparently due to novarsenobenzol and bismuth. The withdrawal of these drugs may well have had as beneficial an effect as the liver extract. Bonsdorff argues that because the white count rises in pernicious anemia following liver therapy it should also rise in agranulocytosis. Yet the mechanism of the leukopenia of pernicious anemia is as yet not clear. It may well be that it is similar to that which produces the anemia in leukemia, namely a crowding out of one series of cells by the overgrowth of another. If this be so, liver therapy would cause a rise of the white blood cell count in pernicious anemia by an indirect rather than a direct method. At present the ultimate value of liver therapy in agranulocytosis cannot be estimated. It can only be said that a few patients have been successfully treated. There would appear to be less evidence for the effectiveness of liver extract than there is for pentnucleotide. Either the one or the other, or neither, may ultimately prove to be of value. At present a larger number of cures have followed pentnucleotide than any other form of therapy, but the drug must be given in the correct dosage to the correct disease.

One author has suggested that the sole hope for the granulopenia patient is sepsis. I can only say that that hope is all too often fulfilled. That sepsis raises the white count in the presence of a normal bone marrow is no

evidence that it will or can stimulate a paralyzed bone marrow to activity. One of my cases developed agranulocytosis in the midst of an attack of boils. It would be far better in my opinion to do all we can to avoid infection.

It appears to me that at present the best method of treating true agranulocytosis is by intelligent nursing care, adequate fluids and food, the careful avoidance of sepsis, if possible, and the administration of full doses of pentnucleotide. Such imperative surgical measures as would be instituted in patients with a normal blood should be used fearlessly in agranulocytosis. Codeine is the best sedative. The future only will tell whether this régime is the most effective. It may well be that some other drug will be found far more effective.

CYCLICAL AGRANULOCYTIC ANGINA *

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Although Franke [1] in 1930 was able to find only three instances of the recurrence of attacks of agranulocytic angina, there are at the present time numerous reports of this condition in the literature. In a few instances these episodes of agranulocytosis have been cyclical in character.[2, 3, 4, 5, 6] One of these cyclical cases [6] has had recurrences simultaneously with the menses. During the past two years we have had under constant observation a patient who has presented this unusual picture of recurrences of granulocytopenia with each menstrual period. A brief report of the main findings in this patient has been made previously.[7] The purpose of this paper is to give the results of our studies of this patient in more detail in the hope that the data may be of some use in the further study of this disease of obscure etiology.

Case Report

Mrs. G. K., a 38 year old, white widow was observed in her first attack of granulocytopenia in November 1932. She had previously been seen on several occasions in the Out-Patient Department because of symptoms of mild hypertrophic arthritis and repeated attacks of urticaria and migraine. In February 1930, she had been admitted to the hospital because of an especially severe attack of urticaria. She gave a history of having taken daily doses of aspirin or amidopyrine for headache for several weeks. It is of interest that at this time, the total white blood cells numbered 7600 per cu. mm., with differential formula as follows: Polymorphonuclear neutrophiles 65 per cent, lymphocytes 33 per cent, monocytes 2 per cent. Skin tests for a number of foods and other substances, including amidopyrine, acetylsalicylic acid and neocinchophen were uniformly negative. In September 1931, cholecystectomy was done because of chronic cholecystitis and cholelithiasis. At this time the white blood cell count was 8600 per cu. mm., with the following differential leukocyte formula: polymorphonuclear neutrophiles 73 per cent, lymphocytes 19 per cent, monocytes 7 per cent, eosinophiles 1 per cent. During the following year she remained well except for frequent headaches (migraine) and dysmenorrhea, for which she took amidopyrine, acetylsalicylic acid and sodium amytal. The exact dosage and frequency with which these were used is not known.

On November 3, 1932 the patient was again admitted to the hospital. Six days before, during the menstrual period, there had been sudden onset of an acute illness, characterized by chills, fever, headache, malaise, anorexia and sore throat. On examination she appeared to be acutely ill. The temperature was 37.5° C., pulse 90, respirations 20. The pharynx was diffusely reddened and edematous. Cervical lymph nodes were moderately enlarged. There were no other physical findings of significance. Throat culture showed a mixed flora with 20 per cent *Streptococcus hemolyticus*. The urine showed no abnormalities. Blood counts on admission were

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as follows: red blood cells 3,850,000 per cu. mm., hemoglobin 11.0 gm. per 100 c.c. of blood, white blood cells 2000 per cu. mm. Of the latter, 14 per cent were polymorphonuclear neutrophiles, the remainder non-granular cells. Local treatment of the throat was instituted and daily injections of pentnucleotide K–96 were begun. During the first three days in the hospital the temperature varied between 37° and 38.5° C. By November 9 the temperature had returned to normal and the throat symptoms had subsided. At this time the leukocytes numbered 6800 per cu. mm., of which 59.5 per cent were neutrophiles. Leukocyte counts during this attack and during the following two years are shown graphically in figure 1.

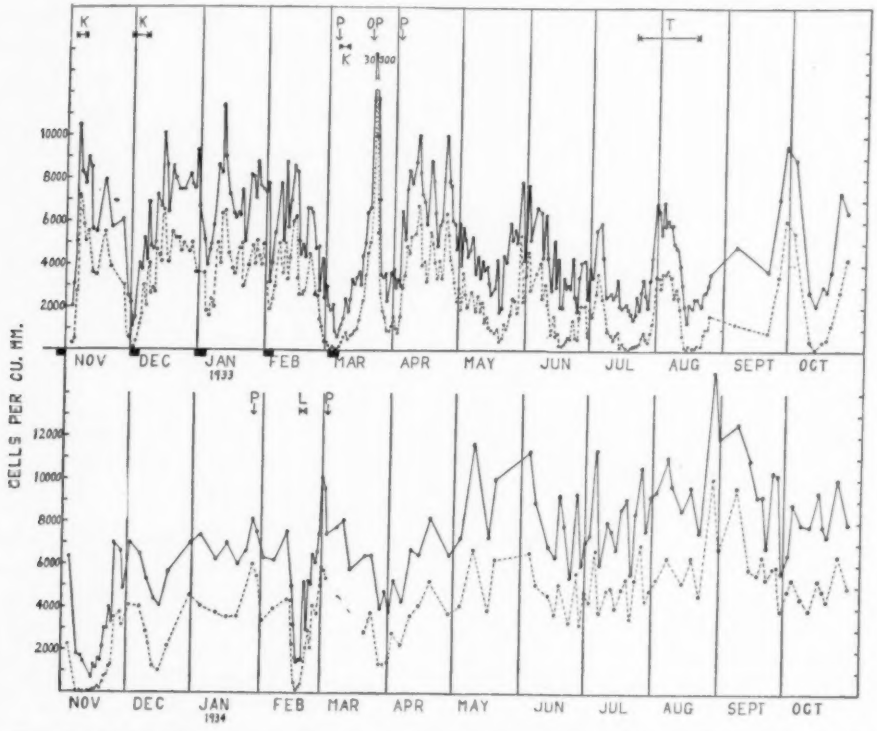

FIG. 1. Solid line: total leukocytes. Broken line: neutrophiles. The areas blocked in black represent the menstrual periods. *K*—pentnucleotide K–96, 20 c.c. daily intramuscularly. *P*—amidopyrine, five grains by mouth. *OP*—bilateral salpingo-oöphorectomy. *T*—theelin. *L*—Lederle's parenteral liver extract, 6 c.c. daily intramuscularly.

On November 29, two days before the onset of the menstrual period, the patient was again admitted to the hospital because of a decreasing leukocyte count. At this time the white blood cells numbered 2900, with 19 per cent granular cells. There were no symptoms with the exception of fatigue which was attributed to overwork. Pentnucleotide was again given in doses of 10 c.c. intramuscularly twice daily and continued for eight days, at the end of which time the leukocyte count was normal. On December 7, a biopsy of sternal bone marrow was obtained. The bone marrow appeared to be essentially normal, except for an apparent decrease in the number of megakaryocytes. There was an abundance of myeloid cells in all stages of development.

In the middle of December, the patient developed a furuncle of the left nostril, slight swelling of the left side of the face and a tender, enlarged lymph gland in the

left anterior cervical region. During this infection, which subsided in a few days, the leukocyte count remained normal. During the next two months there were no complaints. There were, however, two periods of leukopenia during which the total leukocyte count was less than 4000 per cu. mm., the total granulocytes less than 2000 per cu. mm. Each of these episodes occurred at the time of the menstrual period.

During the last 10 days in February 1933, there was a mild upper respiratory infection, with gradual decrease in the leukocyte count. On March 4, the total white blood cell count had dropped to 900 per cu. mm., with 1 per cent granulocytes. In addition to rhinitis, there was herpes labialis, with swelling, redness and tenderness of the upper lip. The menstrual period had begun the day before. Pentnucleotide was again given. During the next two weeks there was a gradual increase in the number of granulocytes and subsidence of the infection.

At this time the patient had been under observation for five months. With each of five menstrual periods, there had been an attack of neutropenia. Three of these had been of sufficient severity to require admission to the hospital. After much discussion it was decided to induce menopause by surgical procedures. Accordingly, on March 21, 1933, subtotal hysterectomy and bilateral salpingo-oöphorectomy were done by Dr. Karl Wilson. On the morning of the operation the white blood cell count was 9600 per cu. mm. with 81.5 per cent granulocytes. Six hours after operation, the total leukocytes had increased to 30,500 per cu. mm., of which 93.5 per cent were granulocytes. During the next few days, however, there was a precipitous diminution in the total leukocytes and granulocytes. For several days the granulocytes varied between 800 and 1500 per cu. mm. During this time the patient was making an otherwise uneventful recovery from the operation. Microscopic examination of the ovaries showed a relatively large number of corpora fibrosa and an unusual persistence of old corpora lutea. During the period from March 12 to April 15, 1933 the urine was examined daily by Dr. C. A. Elden for the presence of estrin by a method previously described.[8] During the 10 days before operation the 24-hour urine specimens contained an average of about 25 rat units of estrin; for 25 days after operation the average content was 5 to 10 rat units. During this period there were two cycles of neutropenia. There was no apparent relationship between the leukocyte count and the amount of estrin excreted in the urine. Extracts of the patient's urine showed a positive ovulation test on the twenty-second day and on the sixty-second day after operation.

During the next few months there were recurrent periods of neutropenia of varying severity at approximately monthly intervals (figure 1). With the majority of these there were no evidences of infection and admission to the hospital was not necessary during this period. Many of the attacks of neutropenia were, however, accompanied by fatigue, irritability, some general malaise and on a few occasions slight soreness of the throat. The moderate degree of anemia that was present during the early months of observation had been relieved by large doses of iron by mouth. The hemoglobin and red blood cell levels have since remained within normal limits.

For several months after operation there were menopausal symptoms, chiefly in the nature of frequent "hot flashes." Between July 20 and August 3, theelin was administered in daily doses of 3 c.c. intramuscularly. From August 3 to 18 the daily dose of theelin was 2 c.c. During the period of theelin administration there was partial relief of menopausal symptoms but there was no apparent effect on the neutropenic cycle.

On November 13, 1933, it was again necessary to admit her to the hospital because of fever, prostration, and marked soreness of the throat and gums. The throat was beefy red, there was marked gingivitis, moderate enlargement and tenderness of the cervical lymph nodes and an inflamed, tender, thrombosed hemorrhoid. The white blood cell count dropped to 600 per cu. mm. and granulocytes disappeared

entirely from the peripheral blood. Because of the severe reactions which attended the injections of pentnucleotide in three previous attacks in which it had been given, and in view of the fact that spontaneous recovery had resulted from other periods of severe neutropenia, nucleotide was not given. Treatment was limited to local and symptomatic measures. There was gradual increase in the total leukocytes and granulocytes and the manifestations of infection subsided.

In December, there was a period of moderate neutropenia without symptoms. Throughout January 1934 the white blood cell count remained at a normal level, although there was a moderately severe respiratory infection during the latter part of the month. During February, however, sore throat, gingivitis, herpes and fever again appeared and were accompanied by a decrease in the total leukocyte count to 1450 per cu. mm. with 10.5 per cent granulocytes on the seventeenth. During the next three days Lederle's Liver Extract was given intramuscularly in doses of 6 c.c. daily. Again the leukocyte count rose and the symptoms disappeared.

During the first week in March 1934, the patient was requested to omit medicines of all kinds with the exception of codeine, which was necessary for the control of headache. This restriction has been maintained since that time. During the latter part of March there was a decrease in the white blood cells and granulocytes with subsequent gradual increase during the early part of April. Since that time the leukocyte level and the percentage of granulocytes have been within normal limits and the patient has remained well except for occasional headache.

During the two year period from November 1932 through October 1934, we have observed in this patient 11 periods of severe granulocytopenia; five of these were accompanied by fever, lymphadenopathy and evidences of infection of the upper respiratory tract. Symptoms during the other six periods were limited to malaise, fatigue, irritability, and slight sore throat. In addition there were five symptomless periods of less severe granulocytopenia, during which the total number of granulocytes was reduced to a level varying between 1000 and 2000 per cu. mm. Throughout the period from January 1930 to March 1934, frequent doses of amidopyrine and other analgesics and sedatives were taken. On four occasions, amidopyrine was administered to the patient during observation in the hospital (figure 1). No significant change occurred in the trend of the leukocyte level at these times. At least one neutropenic cycle (in March–April, 1934) occurred without antecedent drug ingestion.

Throughout the two year period of observation, during which approximately 400 differential leukocyte counts of 200 cells each were made, eosinophiles were observed in the differential formula on only two occasions. Basophiles and monocytes were present in small numbers during this period; the relative number of lymphocytes varied inversely with the number of neutrophiles.

Discussion

We felt justified in having a bilateral salpingo-oöphorectomy performed for the following reasons. First, the patient was a widow with one child and had no desire for marriage and other children. Second, her age was such that the menopause would occur normally within a few years. Third, the exact coincidence of the menstrual cycle and the period of granulocytopenia on repeated occasions was so striking that it seemed reasonable to assume that there *might* be some causal relationship even though similar cyclical recurrences had been observed in the male.[3] Fourth, the patient was perfectly willing to have the operation performed as an experiment.

The effect of the oöphorectomy is difficult to evaluate. Cyclical recur-

rences were present for one year after operation. However, the general shape of the curves representing the total number of white blood cells and the absolute number of neutrophiles in the blood stream underwent some changes during this period. On the whole, the average total number of cells was less and so far as this goes suggested that granulopoiesis was inhibited by this operation. Nevertheless, after this postoperation period of one year there has been no recurrence for 10 months. The question naturally arises as to whether the omission of amidopyrine was responsible for the disappearance of the recurrences. We cannot answer this. Certain it is that amidopyrine was taken at repeated intervals during the period of recurrences without any demonstrable effect on the white blood cell picture. It is unfortunate that we have no accurate record of the amount of this drug that was taken at various times. In view of the many reports in the literature since the original papers by Watkins [9] and Madison and Squier [10] suggesting a close relationship between the drug and granulopenia we have been unwilling to give amidopyrine to this patient. We do not feel, however, that the evidence *in this case* justifies any statement to the effect that this chemical agent was the responsible factor. In this connection, Jackson's [11] recent report of the absence of ingestion of pyramidon or related drugs in 44 per cent of his series of cases is of interest.

In connection with the feeling of certain investigators [12] that allergy is a strong factor in these cases, there is confirmatory evidence to be found in the fact that she has suffered from extreme generalized urticaria in the past. Against this idea is the almost total absence of eosinophiles from the peripheral blood of this patient throughout her entire course of illness.

In regard to therapy, we find little evidence in this one patient of any benefit from either pentnucleotide or liver extract. It is true that the periods of granulopenia were of shorter duration and that recovery from them was associated with the presence of more myelocytes in the peripheral blood when one or both of these substances were administered intramuscularly. However, these findings represent no greater variations from the usual response of such patients than one would expect to find in untreated cases.

Our results with regard to the urinary output of the female sex hormone and of an anterior pituitary-like substance are of some interest. In contrast to the findings of Thompson [5] we found absolutely no correlation between the level of the white blood cell count and the number of rat units of female sex hormone secreted in the urine. Prior to oöphorectomy our values were within normal limits (approximately 25 to 26 units daily) at a time when there was well marked granulopenia. Following operation these values dropped to approximately 5 to 10 units daily and remained there even when neutropenia was present. These findings would seem to indicate that the white blood cell picture was independent of the ovarian hormone resulting from follicular activity. Further confirmatory

evidence of this is found in the failure of theelin to produce any change in the white blood cell picture. The results of the repeated determinations of the amount of anterior pituitary-like substance in the urine give only slight room for speculation. The most that can be said in this connection is that a positive test was found at an earlier postoperative date than is usual. That these findings point to any positive connection between this substance and the white blood cell picture, is open to considerable question.

The histological changes in the ovaries of this patient were of the same character as those seen in the ovaries of monkeys following the administration of large quantities of anterior pituitary-like hormone (prolan). In view of this we studied the white blood cell picture of two monkeys for two months while they were receiving 1.0 c.c. antuitrin S (Parke, Davis and Company) daily subcutaneously. No change in the white blood cell formula was demonstrable.

In order to determine whether menstrual periods in normal young women were associated with any comparable changes in the blood picture, we have investigated the total and differential white blood cell counts of six normal young women over a period of two months including two menstrual cycles. No variation greater than normal was present in the white blood cell counts of these individuals. These findings are in accord with those of Smith and McDowell.

The bone marrow findings are of interest since they presented a normal picture. What they would have been at the time of granulopenia we do not know. In this connection, it is of interest that this patient was able to respond to operation by the usual postoperative leukocytosis. This ability to respond normally to stimuli to white blood cell formation at periods after the subsidence of acute granulopenia has been noted previously.[1, 13]

Summary

The findings in a patient with agranulocytic angina manifested by recurrences at the time of the menstrual cycles have been reported. Following bilateral oöphorectomy there was slight change in the picture during a period of one year, after which time no further recurrences occurred.

Amidopyrine was taken at times by this patient but our data do not allow any positive statement as to any causal relationship between it and the cycles of granulopenia.

BIBLIOGRAPHY

1. Franke, O.: Über rezidivierende Agranulozytose, Folia haemat., 1930, xl, 419–426.
2. Leale, M.: Recurrent furunculosis in an infant showing an unusual blood picture, Jr. Am. Med. Assoc., 1910, liv, 1854.
3. Rutledge, B. H., Hansen-Prüss, O. C., and Thayer, W. S.: Recurrent agranulocytosis, Bull. Johns Hopkins Hosp., 1930, xlvi, 369.
4. Doan, C. A.: Neutropenic state; its significance and therapeutic rationale, Jr. Am. Med. Assoc., 1932, xcix, 194–202.

5. THOMPSON, W. P.: Observations on possible relation between agranulocytosis and menstruation with further studies on case of cyclic neutropenia, N. E. Jr. Med., 1934, ccx, 176–178.
6. JACKSON, H., JR., and MERRILL, D.: Agranulocytic angina associated with the menstrual cycle, N. E. Jr. Med., 1934, ccx, 175–176.
7. STEPHENS, D. J., and LAWRENCE, J. S.: Recurrent agranulocytosis, Jr. Clin. Invest., 1934, xiii, 711.
8. ELDEN, C. A.: Method of study and treatment of menstrual disturbances of endocrine origin, Am. Jr. Obst. and Gynec., 1934, xxviii, 179–186.
9. WATKINS, C. H.: The possible rôle of barbiturates and amidopyrine in causation of leukopenic states, Proc. Staff Meetings Mayo Clinic, 1933, viii, 713–714.
10. MADISON, F. W., and SQUIER, T. L.: Primary granulocytopenia after administration of benzene chain derivatives, Central Society for Clinical Research, 6 Annual Meeting, Chicago, Oct. 27, 28, 1933. Reported in Jr. Am. Med. Assoc., 1933, ci, 2076.
11. JACKSON, H., JR.: Relation of amidopyrine and allied drugs to etiology of agranulocytic angina, Am. Jr. Med. Sci., 1934, clxxxviii, 482–486.
12. SCHILLING, V.: The blood picture and its clinical significance, 1929, C. V. Mosby Co., St. Louis, p. 197.
13. HARKINS, H.: Granulopenia and agranulocytic angina, Jr. Am. Med. Assoc., 1932, xcix, 1132–1138.

THE ETIOLOGY AND PREVENTION OF ANEMIA IN PREGNANCY *

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PREGNANCY may be a coincidence in the course of any number of conditions which in themselves cause anemia, such as leukemia, hemolytic jaundice, and chronic blood loss. Furthermore the gravid state may in part be responsible for hemorrhage, pyelitis and puerperal sepsis, each of which may contribute to the development of anemia. Disregarding patients with anemia due to such well recognized causes, there remains a large group of women who during pregnancy develop moderate to severe anemia which has no obvious etiology. Two kinds of such anemia are encountered. One type, hypochromic in character, occurs much more frequently than the second type which is macrocytic, or " pernicious " in morphology.

Hypochromic anemia in non-pregnant individuals is generally believed to be due to a nutritional deficiency. This deficiency may result from a direct dietary lack, or from faulty absorption due to gastrointestinal abnormalities, or from a loss of blood-building materials, as for example, in chronic bleeding. Not infrequently a combination of two or all three of these factors is encountered in any given case.

When women suffering from these defects become pregnant, not only may a preëxisting anemia be much enhanced but severe anemia may develop. In the hypochromic anemia of pregnancy there is seldom significant alteration in leukocytes or blood platelets, but stained films show small pale erythrocytes. The chief presenting clinical symptoms are pallor, lack of a sense of well being and excessive fatiguability. In the very severe cases edema, dyspnea, prostration and syncope may be observed. Rarely is enlargement of the spleen detected.

Thirty patients with this type of anemia in pregnancy were studied,[1] all of whom had severe anemia, with less than 45 per cent hemoglobin (Sahli) (7.02 gm. per 100 c.c.). Rigorous examination failed to reveal concomitant disease or loss of blood. Seventeen of the 30 patients had complete posthistamine gastric anacidity, even when examined after parturition. Ten patients had little or no free hydrochloric acid in the gastric secretion after the usual alcohol test meal, and diminished amounts after histamine stimulation. Two patients only had normal gastric acidity post partum.

With but one exception, all the patients who did not have complete gastric anacidity had partaken of diets poor in iron, not only throughout pregnancy but often over a period of years. Eight of the 17 patients with complete absence of gastric free hydrochloric acid had partaken of good, if not op-

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timal, diets throughout pregnancy, while the remainder had not had an adequate intake of iron-containing foods. It was thus apparent that either gastric secretory defects or diets deficient in iron-containing foods, or both these factors, were present in the patients with hypochromic anemia developing in pregnancy. Recently Davies and Shelley [2] have made a similar study of hypochromic anemia in pregnancy. Two of their 20 patients had normal gastric acidity, the other 18 having hypoacidity or anacidity. Deficient diets were encountered in 14 of the 20 women.

Furthermore it is to be remembered that all of these women had what to them was essentially comparable to chronic blood loss, since the building stones for the fetal hemoglobin are of necessity derived from the maternal organism.[3] No matter how anemic the mothers became, in every instance their infants were born with a normal red blood cell count and a normal amount of hemoglobin.[1] The materials entering into the formation of the fetal hemoglobin are just as certainly lost to the mother as if there were menorrhagia.

The treatment of hypochromic anemia in pregnancy does not differ from the treatment of this condition in non-pregnant patients. Iron in adequate dosage (6 gm. of ferric ammonium citrate or 1 gm. of ferrous sulphate daily in our experience) has resulted in prompt recovery from the anemia in every instance.[1] Hemoglobin is regenerated in the severe cases at a rate of approximately 1 per cent (0.156 gm. per 100 c.c.) per day, irrespective of whether treatment is instituted during or after pregnancy.

The prevention of this type of anemia in pregnancy may probably be accomplished, in the absence of gastrointestinal disturbances, by supplying the pregnant woman with a diet adequate in blood-building materials. A study which is now being carried out [4] indicates that hypochromic anemia may be uniformly prevented by the administration of small doses of ferrous sulphate (0.4 to 0.6 gm.) daily, to pregnant women. In a series of 100 normal pregnant women so treated anemia has not developed, whereas a significant degree of hemoglobin reduction has occurred not infrequently in a control series of 100 normal pregnant women studied under the same conditions as the first group but not given iron.

The prevention and treatment of this form of anemia in pregnancy is important, not only from the viewpoint of the health of the mother, but also that of the child. Although the infants born to women suffering from hypochromic anemia of pregnancy show no reduction in the number of red blood cells or the percentage of hemoglobin at birth, they ordinarily develop hypochromic anemia during their first year of life.[3] This is presumably due to a failure on the part of the fetus to store an adequate amount of blood-building materials during its intra-uterine existence. During that period of neonatal life when its diet is usually restricted to milk, the normal infant draws upon its large supply of iron stored in the liver and other organs, which is probably lacking in infants born of women who are themselves deficient in iron. If, however, the anemic mother is

given sufficient iron before delivery so that her hemoglobin approaches the normal range at or before parturition, hypochromic anemia due to deficient iron storage does not develop in her infant.[3]

Patients with macrocytic or "pernicious" anemia of pregnancy are usually more seriously ill than those with hypochromic anemia. In addition to the symptoms referable to anemia per se, nausea, vomiting and diarrhea are common. Fever, without demonstrable infection, abating when specific anti-anemic therapy is employed, occurs in most cases. Soreness of the tongue, splenomegaly and neural signs are occasionally encountered. Gastric anacidity or hypoacidity occurs in about 50 per cent of cases.

The examination of the blood shows that the number of erythrocytes is more markedly diminished than the amount of hemoglobin so that the color index is usually above 1. Moderate variation in size and shape of the red blood cells on stained blood films is the rule. Macrocytes, microcytes and tailed forms are frequent. Megaloblasts are rarely seen except in the early stages of remission.

Mean corpuscular volume determinations show a somewhat increased cell size (from 105 to 130 cubic microns), on the average not so marked as in Addisonian pernicious anemia. The concentration of hemoglobin in the red blood cells is frequently slightly reduced. The leukocytes and blood platelets are either normal or slightly decreased. A relative increase of lymphocytes accompanies the leukopenia in most cases. The serum color is either normal or slightly more yellow than normal.

There is evidence which suggests that this anemia is a manifestation of the same kind of nutritional deficiency state as exists generally in anemias of the pernicious type. Studies of these patients have shown that the same etiologic mechanisms produce this type of anemia in pregnancy as are active in non-pregnant patients. Certain of the women apparently develop the deficiency state as a result of inadequate diet alone[5]; in others a virtual deficiency develops because of a lack of Castle's "intrinsic factor" of the gastric juice[1]; and in many there is reason to believe that a combination of both these causes is responsible.[1] Clear-cut evidence pointing to defective absorption as an etiologic factor in this type of anemia in pregnancy is lacking, but it seems probable that this is involved in certain cases.

Macrocytic (pernicious) anemia of pregnancy may be relieved by the administration of materials potent in Addisonian pernicious anemia. When treatment is instituted during pregnancy much larger doses of potent material than are usual in the average case of Addisonian pernicious anemia may be required. For patients who do not respond readily to potent material administered orally, liver extract should be injected. Daily injections of as much as 5 to 10 c.c. of Solution Liver Extract Lilly (N.N.R.) have been required in certain cases in order to produce remission.

Summary

1. The hypochromic anemia of pregnancy is due either to a direct dietary deficiency or to a deficiency conditioned by gastric anacidity, hypoacidity or associated gastrointestinal defects in the presence of the fetal demand for blood-building materials. It may be completely relieved, either during or after pregnancy, by the administration of iron in suitable (usually large) doses.

2. The macrocytic anemia of pregnancy may be due to a temporary lack in the gastric juice of a specific intrinsic factor, to direct dietary deficiency, or to a combination of these factors. It may possibly result at times from disturbances of intestinal absorption. It can be relieved either during or after pregnancy by the administration in adequate dosage of materials potent in Addisonian pernicious anemia.

3. The development of anemia in pregnancy may best be prevented by supplying the pregnant woman with an adequate intake of blood-building materials.

BIBLIOGRAPHY

1. Strauss, M. B., and Castle, W. B.: Studies of anemia in pregnancy, III, Am. Jr. Med. Sci., 1933, clxxxv, 539–551.
2. Davies, D. T., and Shelley, U.: Some observations on hypochromic anaemia and its relation to pregnancy, Lancet, 1934, ii, 1094–1099.
3. Strauss, M. B.: Anemia of infancy from maternal iron deficiency in pregnancy, Jr. Clin. Invest., 1933, xii, 345–353.
4. Dr. John C. Corrigan, Boston.
5. Wills, L.: Treatment of "pernicious anaemia of pregnancy" and "tropical anaemia' with special reference to yeast extract as curative agent, Brit. Med. Jr., 1931, i, 1059-1064.

A STUDY OF NINE CASES OF BRONCHOMONILIASIS *

By JOHN W. FLINN, M.D., F.A.C.P., ROBERT S. FLINN, M.D., F.A.C.P., and ZEBUD M. FLINN, M.D., *Prescott, Arizona*

MONILIA may be regarded physiologically as true yeasts since they too ferment sugars with the production of gas. Morphologically, however, they differ from true yeasts (Saccharomyces) in that they have a vegetative body (mycelium), consisting of a collection of fine filaments or threads (hyphae) and reproduce by free-born spores (conidia). True yeasts have no definite mycelium and they reproduce by ascospores. Consequently the genus, Monilia Persoon is very generally placed in the class, Fungi imperfecti (Hyphomycetes). It is further classified in the family Oosporaceae Saccardo, as its spores are arranged in chain-like formation. Further morphological differentiation has not been made and classification into genus and species is based on biochemical reactions in fermenting sugars.

Bronchomoniliasis is a disease of the respiratory tract caused by any species of the genus Monilia. The first reported case was by Castellani from Ceylon in 1905. Boggs and Pincoffs of Baltimore reported the first case in the United States in 1915. A review of medical literature in 1931 showed only 11 additional reports in the United States up to that time. None of our cases are included in these figures.

The first case we recognized was referred to us in January 1924, from Wheeling, West Virginia, with a diagnosis of advanced pulmonary tuberculosis. Repeated examinations of the sputum were negative for tubercle bacilli and we made a tentative diagnosis of unresolved pneumonia. Several months later while culturing the sputum for an autogenous vaccine we, quite by accident, stumbled on some yeast cells on a neglected plate of culture medium. These yeast cells were subcultured and later classified by their morphology, their cultural characteristics and biochemical reactions in the genus Monilia.

In the meantime these microörganisms were injected into the lungs of rabbits and produced typical lesions, which will be referred to later. Cultures from these lesions showed an organism with the same characteristics and chemical reactions as those isolated from the patient's sputum. We therefore felt justified in making a definite diagnosis of bronchomoniliasis.

We then issued strict orders in our laboratory that a thorough search for fungi, including cultural study, be made on any sputum in which repeated examinations failed to show tubercle bacilli. In this way we have since picked up eight other cases of uncomplicated bronchomoniliasis, which otherwise would probably have been overlooked. The same diagnostic methods were followed as in case 1.

* Read at the Chicago meeting of the American College of Physicians, April 20, 1934.

It was not until 1933 that we began to determine with what species of Monilia we were dealing. Further study of their biochemical reactions in fermenting sugars enabled us to classify the microörganisms in our last two cases in the species *Monilia Pinoyi*. One of these cases came to autopsy and the same species of monilia was recovered from the pleural fluid, lungs and brain. Autopsy findings are reported later.

Classification

Table 1 shows the classification of microörganisms that we have tentatively adopted. It follows somewhat closely that suggested by Castellani, and seems to us the most practical classification obtainable at present. Its general principles were indicated in our opening paragraph.

Table I

Classification of Microörganisms

	Thallophyta (thallus)	Spermatophyta (seed)	Ptendophyta (fern)	Byrophyta (moss)
Subdivisions	Fungacae (saprophytic and parasitic)	Algae (chlorophyll)		
Divisions	Fungi (higher)	Bacteria (lower fungi)	Vegetative bodies	
	Eumycetes (fungi found in man; filamentous forms; single nuclei)			
Class	Fungi imperfecti (Hyphomycetes) yeast-like fungi; free-born spores			
Order	Thallosporales (thallus reproduction; mycelial hyphae)			
Suborder	Blastosporinae (asexual, oval budding forms)			
Family	Oosporaceae Saccardo (formation of chain-like spores)			
Genus	Monilia Persoon (sugar fermentations; gas formation; budding forms in culture)			
Species	*Monilia Pinoyi* (sugar reactions; pathogenicity to animals)			

Mycology

Figure 1, *a, b, c, d,* shows photomicrographs of cultures of *Monilia Pinoyi* at different periods of growth. Figure 1*a* (48 hours) shows yeast-like fungi with budding forms (class, Fungi imperfecti). In figure 1*b* (3 days) we see beginning division of the free-born spores. Figure 1*c* (5 days) shows the formation of mycelial hyphae (order Thallosporales). Figure 1*d* (15 days) shows the formation of chain-like spores (family Oosporaceae Saccardo) and mycelial hyphae.

Table 2 shows the further classification of these organisms into the genus Monilia Persoon by their ability to ferment glucose and form gas and finally into the species *Monilia Pinoyi* by their sugar reactions and pathogenicity to laboratory animals.

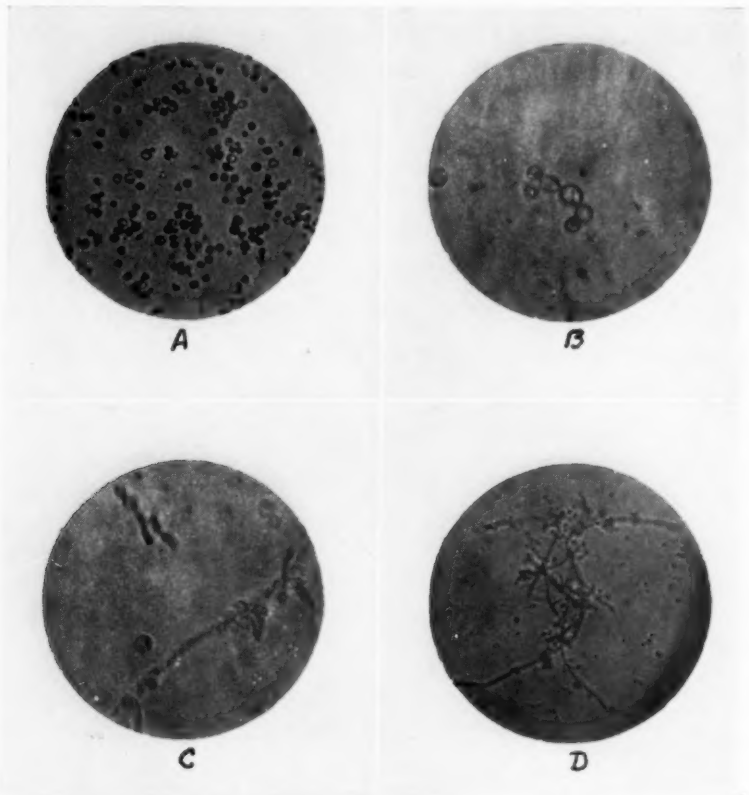

FIG. 1. Cultures of *Monilia Pinoyi*. (*a*) Forty-eight hours' growth showing yeast-like fungi with budding forms. (*b*) Three-day growth showing beginning division of the free-born spores. (*c*) Five-day growth showing the formation of mycelial hyphae (order Thallosporales). (*d*) Fifteen-day growth showing the formation of chain-like growths (family Oosporaceae Saccardo).

LABORATORY DIAGNOSIS

Monilia may be found very frequently in the normal mouth and throat so that the mere presence of monilia in sputum is not sufficient evidence to establish a diagnosis of bronchomoniliasis. Precautions should be taken to prevent contamination of the sputum from an outside source and the mouth and throat should be cleansed by gargling before collection of sputum.

A positive diagnosis of bronchomoniliasis is justified only by the constant finding of a pathogenic monilia species in the expectorated sputum. The pathogenicity of the organisms and their causative relationship to the disease in question can be proved only when their intra-pulmonary inoculation in rabbits results in the production of small pulmonary nodules. Microscopically, these nodules show a picture seen in other species of granulatomatous processes and consist of leukocytes, epithelioid and giant cells

TABLE II

Subclassification into Genus and Species

Organism No.	Source	Morphology	Color			Plain Broth	Odor of Cultures	Pathogenicity	Character of Growth	Motility	Gram Reaction	Dextrose	Levulose	Maltose	*d*-Galactose	Saccharose	Mannite	Lactose	Dextrin	Rhamnose	*l*-Arabinose	Adonite	Inulin	Sorbite	Starch	Glycerine	Gelatine	Serum	Litmus Milk
			Lead Acetate	Sabouraud's	Nutrient Agar																								
1	Sputum Case 8	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty	Killed a rabbit in 21 days	Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Brain Case 8	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty		Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	Rabbit Org. 1	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty	Organism No. 1	Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	Sputum Case 9	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty	Killed a rabbit in 7 days	Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	Left lung Case 8	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty		Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Rt. lung Case 8	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty		Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	Rabbit Org. 4	Yeast-like mycelium	White Pasty	White Pasty	White Pasty	Sediment	Yeasty	Organism No. 4	Raised Slowly	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

with or without a central area of necrosis. The periphery is usually composed of fibroblastic elements. In addition to these tubercles there may be present a generalized hyperemia throughout the affected pulmonary tissues, associated with a parenchymatous and interstitial edema of the alveolar epithelium and a narrowing of the alveolar tubules. Monilia must be recovered from these lesions.

Clinical Diagnosis

Symptomatology. Table 3 summarizes the outstanding symptoms in our nine cases. The age varied from 21 to 58 with an average of 35.5 years, confirming the observations of others that most cases occur in adults. The cases were almost equally divided between males and females. The duration of the disease had been from four to seven years in four cases and from four months to two years in five cases. The onset was influenzal-like in five cases. Pleurisy was the initial symptom in three cases. In the one remaining case the attack began with an hemoptysis. Severe cough was a prominent symptom in the majority of cases, being paroxysmal in character and especially troublesome at night.

In general there was nothing characteristic about the expectoration. In one case there were large amounts of bloody frothy sputum for many months, in another the patient noted a sweetish taste to the sputum, while in another case the sputum had a distinct yeast-like odor. In only two cases was there frank hemoptysis. In four cases there was no loss of weight; in three the loss of weight was moderate and in only two cases was it marked. Fatiguability was not an outstanding symptom. In general, pain was a rather prominent symptom. Shortness of breath was present in all cases except two. In the others it was a prominent symptom. Night sweats were present in about half of the cases. Weakness was rather an outstanding symptom, being prominent in seven cases.

The lesion was confined to the lower lobes in seven cases; in one of these the lesion was in the left lower lobe. In the remaining six it was located in the right lower lobes. In only one case was the lesion confined to the apices. In two cases the entire lung was affected; in one of these the process was bilateral.

Geographically the patients came from all sections of the United States. In general, the symptomatology is that of any chronic pulmonary infection. Although certain symptoms such as paroxysmal cough, chest pain and shortness of breath are prominent they are not sufficiently characteristic to be of much value in establishing a diagnosis. The fact that these are predominatingly basal lesions would in itself suggest that they are non-tuberculous.

Blood Picture. Contrary to some reports, marked changes in the blood picture were not present, there being eosinophilia in only one case and

TABLE III

Clinical Findings

Case	Locality	First Consult.	Age	Sex	Symptoms Began	Initial Symptoms	Cough	Expectoration	Hemoptysis	Lost Weight	Tiredness	Pain	Short Breath	Night Sweats	Weakness	Lesion in:	Outcome
1	W. Va.	Jan. 1924	52	F.	4½ yrs. ago in W. Va.	Acute influenzal	Very severe	Considerable	Continuous	None	Marked	Moderate	On exertion	None	Marked	Rt. middle lobe	Died Jan. 1925
2	Va.	Jan. 1925	21	M.	4 yrs. ago U.S. Navy	Pleurisy and bronchitis	Severe	Considerable	Sputum tinged	None	Moderate	Constant	On exertion	Slight	Marked	Rt. lower lobe	Unknown
3	Mo.	June 1925	31	M.	6½ yrs. ago U.S. Army	Pleurisy and effusion	Severe	Considerable	Sputum tinged	Marked	No complaint	In spine	Considerable	Moderate	Moderate	All lobes	Complete recovery
4	Mich.	Sept. 1925	24	M.	7 yrs. ago in France	Acute influenzal	Severe	Considerable	Severe	None	No complaint	None	Considerable	None	No complaint	Rt. lower lobe	Improved and lost sight of
5	Calif.	Nov. 1925	30	F.	1 yr. ago in Calif.	Acute influenzal	Severe	Slight amount	None	None	Considerable	None	On exertion	None	Slight	Rt. middle lobe	Improved and lost sight of
6	Ore.	Nov. 1926	31	F.	6 mos. ago in Oregon	Hemoptysis	Slight	Slight amount	Small	Moderate	No complaint	Slight	No complaint	Moderate	Considerable	Rt. lower lobe	Improved and lost sight of
7	Calif.	Nov. 1926	26	F.	4 mos. ago in Calif.	Acute influenzal	Very severe	Slight amount	None	Moderate	Considerable	Moderate	Noticeable	Moderate	Considerable	Left lower lobe	Complete recovery
8	Ill.	June 1933	47	M.	2 yrs. ago in Illinois	Pleurisy	Very slight	Very slight	None	Marked	Marked	Severe	Very marked	None	Very marked	Both pleurae Both upper lobes	Died July 1933
9	Ariz.	July 1933	58	M.	4 mos. ago in Ariz.	Acute influenzal	Considerable	Considerable	None	Moderate	No complaint	Severe	None	None	Considerable	Rt. lung. all lobes	Complete recovery

moderate secondary anemia in two cases. Definite leukocytosis was present in two cases. The Wassermann reaction was negative in all nine cases.

Physical Signs. The physical signs were rather indefinite. In the seven basal lesions the percussion note was dull with diminished breath sounds and an absence of definite râles in many cases. The apical lesions showed a greater tendency toward bronchial breathing and increased breath sounds; and definite fine crepitations were a more constant finding than at the base.

Roentgen-Ray Findings. We found no characteristic roentgenological picture. Suggestive findings were that the lesions were confined largely to the base, that the right lung was more affected than the left and that in all but two cases the apices remained clear. The shadows varied from a few rather dense infiltrative strands extending into the periphery of the lung, to homogenous densities occupying the greater part of the lung field. In some cases there were diffuse strands of stringy woolly density which were unlike any other basal lesion which we have seen and may prove to be of value in differentiating this from other basal lesions.

Prognosis

Of the cases which responded promptly to treatment four may be classified as mild, one as intermediate and one as advanced. Of the two cases which showed no improvement whatever under treatment both were far advanced. The remaining case was lost sight of immediately after the examination was completed and before treatment was instituted.

Treatment

All the patients were put on quite intensive bed rest. All were given potassium iodide in increasing doses. Most of these patients could tolerate as much as 75 grains daily but beyond this point gastrointestinal symptoms usually developed. We did not find it necessary to resort to the intravenous or intramuscular use of iodine preparations.

Following the practice of Ashford in the treatment of intestinal moniliasis (sprue) and based on our observation that *Monilia Pinoyi* does not ferment lactose, all commercial sugars were eliminated from the diet in case 9 and milk sugar was substituted. This patient made a spectacular recovery, but since potassium iodide was also given it is difficult to determine what, if any, effect was exerted by the lactose.

Case VIII

Dr. G. W., aged 47, was referred to us in June 1933 with a diagnosis of pulmonary tuberculosis. Both the past history and the family history were essentially negative. In August 1931 he developed a pain over the anterior left chest while playing golf. At one of the larger clinics in this country a diagnosis was made of probable malignant growth in the right lower lobe. He continued to work until

TABLE IV

Blood Pictures

Case	Hemoglobin	Red Blood Cells	White Blood Cells	Polynuclears	Eosinophiles	Basophiles	Small Lymphocytes	Large Lymphocytes	Total Lymphocytes	Large Mononuclears	Transitionals	Total Monocytes	Wassermann	Urine
1	75	5080000	10950	35.5	6.5	1	4.5	49.5	54	2	1	3	Negative	Negative
2	100	5220000	8000	49.0	2.0	0	16.0	32.0	48	0	1	1	Negative	Negative
3	88	4800000	15200	78.0	2.0	0	0.0	18.0	18	0	2	2	Negative	Negative
4	83	4844000	6600	56.0	0.0	0	0.0	0.0	43	0	1	1	Negative	Negative
5	95	4744000	12400	74.0	0.0	0	15.0	8.0	23	0	3	3	Negative	Negative
6	80	3824000	10000	61.0	0.0	0	37.0	2.0	39	0	0	0	Negative	Negative
7	90	4272000	10000	75.0	2.0	2	11.0	8.0	19	0	2	2	Negative	Negative
8	67	3280000	5450	54.0	4.0	0	31.5	2.5	34	7.5	.5	8	Negative	Negative
9	84	4720000	8750	53.5	2.0	1	37.5	3.5	41	2	.5	2.5	Negative	Negative

the spring of 1932 when he visited a number of the larger clinics of Europe. There the consensus seemed to favor a diagnosis of malignancy.

He returned to work in the fall of 1932 at which time he began to run a fever and to feel badly for the first time. In November he became very ill and entered a Chicago hospital where fluid was twice removed from the right pleural space. For the first time a definite diagnosis of malignancy of the right lung was made and a hopeless prognosis given. Following the removal of fluid the patient improved rapidly and gained 20 pounds in weight. In March 1933 he came to Arizona. Shortly after his arrival he again became acutely ill and it was discovered that he had an effusion in the left pleural space. The fluid was removed on two occasions and air substituted. During this time there was no cough or expectoration although the patient complained of chest pain and was intensely dyspneic. On one occasion the patient raised a small amount of sputum which was reported to have contained tubercle bacilli. (In view of the subsequent developments this was probably a technical error.)

When he first came under our observation he was weak and emaciated. The most outstanding symptom was intense dyspnea. He had little cough, occasionally raised sputum, but complained of no chest pain. Perhaps the most striking feature of the case was that during the time he was under our observation the temperature was never above normal. There were many coarse râles over the right lower lobe with marked dullness over the left lower lobe. A few days later the patient expectorated a small amount of sputum which was negative for tubercle bacilli but contained a number of monilia which subsequently proved pathogenic for laboratory animals. Examination of fluid removed from the left pleural space showed monilia which also proved pathogenic on animal injection. Potassium iodide was given in large doses with no favorable effect. The patient grew steadily worse and died on August 24, 1933. A few days before death he developed violent noisy delirium which could be controlled only by large doses of narcotics.

Autopsy

Autopsy findings, two hours after death. The body was that of a moderately emaciated white male. External examination of body showed no marks except an old healed scar in the right lower quadrant. The muscles were small and atrophic.

The scalp, periosteum and skull cap were negative. On removing the skull cap there was apparently an increase in the cerebrospinal fluid. The longitudinal sinus and the meningeal vessels appeared engorged with blood. The surface of the brain appeared markedly congested, all fissures between the convolutions and the sub-pial space being filled with a bloody exudate. In the most marked areas there appeared many small white masses. On section of the brain all vessels appeared congested and there was an increase of fluid in the lateral sinuses. The choroid plexus appeared matted together.

Heart. The pericardium was negative except for adhesions to both lungs. There was a moderate amount of fat over the surface of the heart. The muscles were relatively firm. On section there was no gross change. The middle cusp of the mitral valve was thickened. The coronary vessels were negative.

Right Lung. The pleura was markedly thickened and was adherent at intervals over the entire lung surface producing a series of pockets which, however, contained no fluid. The upper half of the upper lobe showed an area suggesting beginning consolidation but soft in consistency and hyperemic.

Left Lung. The pleura was thickened to the same extent as on the right. The lung was about one-half collapsed and the pleural cavity contained 1000 c.c. of fluid. A wide band of adhesions extended along the third rib from the sternum to the axilla. The upper part of the left upper lobe presented the same appearance as that of the

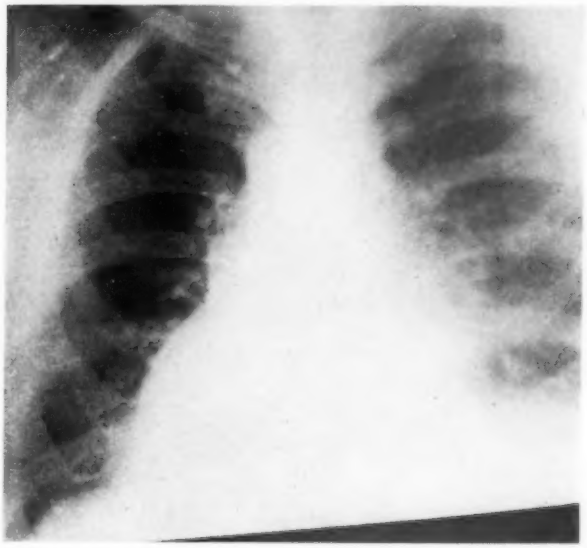

FIG. 2. *Case 9* (April 7, 1933). Suggestive "stringy woolly" shadows throughout the lower right lung field.

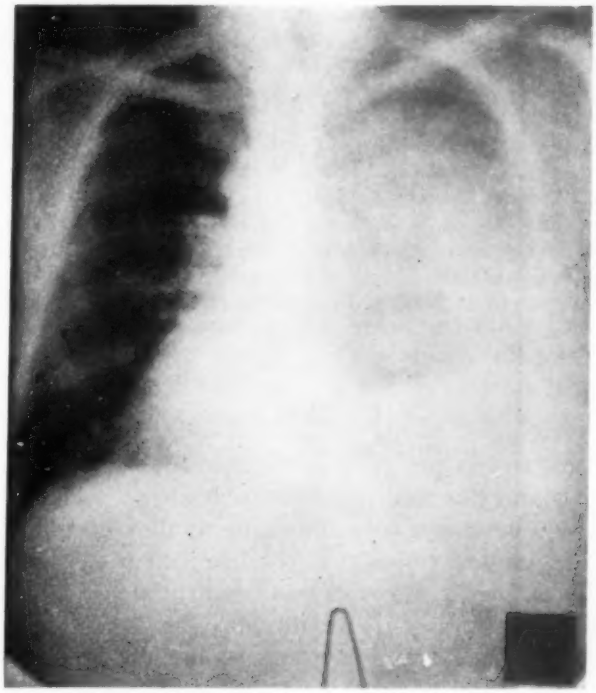

FIG. 3. *Case 9* (July 1, 1933). Kidney-shaped homogeneous shadows covering entire left lung field.

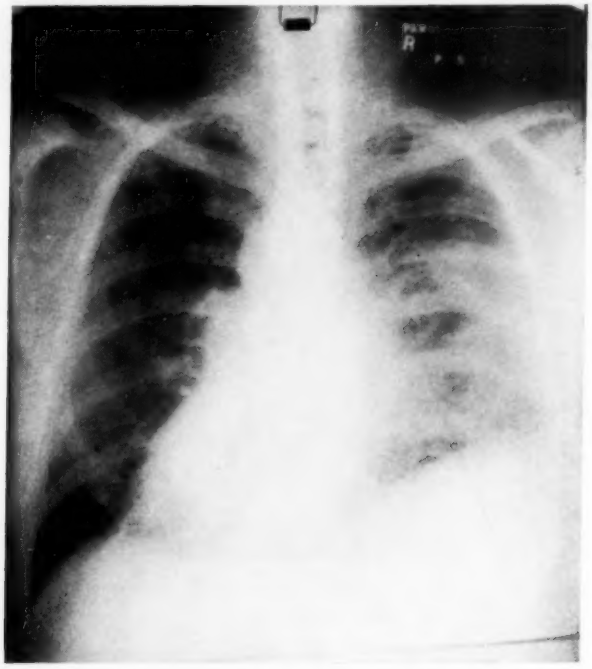

FIG. 4. *Case 9* (August 31, 1933). Following the use of potassium iodide. Clearing of the right lung with persistence of the "stringy woolly" shadows especially at the right base.

right. The lower lobe presented no gross changes. The bronchi were dilated to a slight extent and presented the appearance of mild bronchiectasis. The bronchial glands were not enlarged and showed no pathologic change. The pulmonary vessels of the upper lobes were congested. Liver and spleen showed passive hyperemia. The other organs were essentially normal.

Postmortem Bacteriological Report. Cultures were made at autopsy from the small white areas on the brain surface, from the choroid plexus, from the left pleural space and from the pneumonic areas in both upper lobes. Without exception all cultures yielded a growth of *Monilia Pinoyi* which upon injection into the pulmonary tissue of rabbits produced characteristic granulomatous nodules. Cultures from these nodules yielded *Monilia Pinoyi.*

CONCLUSIONS

Bronchomoniliasis is probably a widespread disease and occurs in all sections of this country as well as in the tropics.

Many cases go unrecognized, simulating as they do pulmonary tuberculosis in its various clinical forms. Early diagnosis is exceedingly important. In its early stages the disease responds beautifully to treatment, but in its advanced stages the prognosis is usually hopeless.

The final diagnosis is entirely dependent on laboratory findings including animal inoculation. If this disease is to be generally recognized it is quite necessary that repeated examinations including cultural studies be made on all questionable sputum.

BIBLIOGRAPHY

1. Castellani, A.: Fungi and fungous diseases, Arch. Dermat. and Syph., 1927, xvi, 383, 571, 714; 1928, xvii, 61, 194, 354.
2. Stovall, W. D., and Pessin, S. B.: Classification and pathogenicity of certain monilias, Am. Jr. Clin. Path., 1933, iii, 347–365.
3. Shaw, F. W.: Monilia from respiratory tract, Jr. Lab. and Clin. Med., 1927, xii, 968–972.
4. Lewis, S. J.: Moniliasis of lungs and stomach, Am. Jr. Clin. Path., 1933, iii, 367–374.
5. Henrici, A. T.: Molds, yeasts and actinomycetes, 1930, John Wiley and Sons, Inc., New York.
6. Jacobson, H. P.: Fungus diseases, 1932, Charles C. Thomas, Baltimore.
7. Hoffstadt, R. E., and Lingenfelter: Pulmonary infection caused by Monilia balcanica (Castellani), Am. Jr. Trop. Med., 1929, ix, 461–467.
8. Boggs, J. R., and Pincoffs, M. C.: A case of pulmonary moniliasis in the United States, Johns Hopkins Hosp. Bull., 1915, xxvi, 407–410.
9. Kotkis, A. J., Wachawiak, M., and Fleisher, M. S.: Relation of monilia to infections of upper air passages, Arch. Int. Med., 1926, xxxviii, 217–221.
10. Haythorn, S. R., Robinson, G. H., and Johnson, L.: Report of a case of early Hodgkin's disease secondarily infected with strain of pathogenic Monilia, Ann. Int. Med., 1932, vi, 72–81.
11. Smith, L. W.: Rôle of monilia psilosis (ashfordi) in experimental sprue, Jr. Am. Med. Assoc., 1924, lxxxiii, 1544–1549.
12. Galbreath, W. R., and Weiss, C.: Bronchomoniliasis, Arch. Int. Med., 1928, xlii, 500–507.
13. Stovall, W. D., and Greeley, H. P.: Bronchomycosis, Jr. Am. Med. Assoc., 1928, xci, 1346–1351.
14. Grossi, G., and Ballog, P.: Clinical and experimental studies in Castellani's pulmonary moniliasis, Jr. Trop. Med., 1929, xxxii, 253–262.
15. Warr, O. W.: Bronchomoniliasis; clinical and pathological study, with report of illustrative cases, Ann. Int. Med., 1931, v, 307–332.

THE TREATMENT OF ACUTE MERCURIC CHLORIDE POISONING *

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In 1915 Lambert and Patterson [1] proposed a method of treatment for bichloride poisoning, designed primarily to accelerate the excretion of mercury from the body. Since that time the gradual acquisition of knowledge concerning this intoxication has led to innovations in its therapy. Various workers have from time to time advocated procedures designed to prevent certain of the toxic effects of mercury, and to combat certain of the physiologic disturbances occasioned by its presence in the body.

Naturally, a large part of the investigations in the therapy of mercury poisoning has centered about the search for chemical antidotes, which would prevent the absorption of mercury or render innocuous that which has been absorbed. Among the substances recommended have been calcium sulphide,[2] sodium phosphite,[3] sodium hypophosphite and hydrogen peroxide,[4] acacia,[5] hydrogen sulphide [6] and sodium thiosulphate.[7] While it is likely that some of these substances prevent the absorption of mercury to a certain extent, it is decidedly improbable that any of them mitigates the toxic effect of absorbed mercury.

The method of treatment proposed by Lambert and Patterson [1] was based on the premise that the chances of recovery might be enhanced by the rapid elimination of mercury from the body. Large volumes of fluid were given by mouth and by rectum in order to sweep mercury out through the kidneys; the stomach and colon were washed out frequently to remove mercury excreted into them. Alkaline salts were given by mouth and by proctoclysis, possibly to combat the acidosis of mercury poisoning, but more likely because of their diuretic effect.

The first treatment frankly aimed at rectification of disturbed physiology was introduced by Weiss,[8] who administered alkali by mouth and by vein to combat the acid intoxication [described by MacNider [9]] and who advocated the use of hypertonic salts to reduce "colloidal swelling of the tissues." [10]

In 1916 Lewis and Rivers [11] and in 1917 Campbell [12] reported marked reduction of plasma chloride in severe mercurial intoxication. Hayman and Priestley,[13] Peters and Van Slyke [14] and Lemierre, Laudat and Laporte [15] advocated parenteral administration of saline to compensate for the chloride deficit.

Haskell, Carder, and Coffindaffer [16] in 1923 demonstrated the value of forcing fluid parenterally in experimental mercury poisoning. In several

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methods of treatment, fluid was forced,[1, 8, 17] but little stress was laid on the employment of parenteral routes of administration.

Shock, the cause of death in almost a fourth of the patients who die from the ingestion of mercuric chloride,[18] was apparently ignored in the older methods of therapy. The first mention, so far as we know, of measures to combat shock in mercury poisoning, was made very recently by Peters, Eisenman and Kydd,[19] who propose a method of treatment, the aim of which is the "prevention or rectification of the functional disturbances caused by mercury."

An analysis of the case records of all patients treated for acute mercury poisoning at Charity Hospital during the last 16 years [302 cases in all[18]] showed that no progress in therapy had been made during this period. Throughout these years, with varying methods of treatment, the mortality remained about 25 per cent. About half of the patients reputed to have taken mercuric chloride developed signs of mercury poisoning, and about half of these died. During the early part of this period, 1917 to 1924, either the Lambert and Patterson method or the Weiss treatment or a combination of the two was used. From 1924 to 1930, the treatment remained unchanged, except that sodium thiosulphate was given to nearly all patients. After 1930, most of the patients were given infusions of 10 per cent glucose daily, and occasionally infusions of normal salt solution, in addition to the other treatment. The mortality was almost exactly the same in cases which were given sodium thiosulphate as in those which did not receive it.

In July 1932, we instituted certain changes in therapy, which seemed logical to us, considering the anatomic lesions and the disturbed physiology of mercury intoxication. The modified form of therapy employs chiefly certain principles of other methods and cannot, therefore, be considered a new treatment. It is, in fact, identical in most details with the form of therapy proposed by Peters, Eisenman, and Kydd,[19] whose work antedates ours. This paper is concerned with the results obtained by this method of treatment in 34 patients who had ingested bichloride of mercury.

Method of Treatment

1. *The Usual Emergency Measures.* Milk is administered, followed by gastric lavage.* A saline cathartic is introduced into the stomach before the tube is withdrawn provided no shock is evident.

2. *Introduction into the Body of an Adequate Amount of Fluid.* For the first 48 hours the amount given is arbitrarily set at 4000 to 6000 c.c. daily. This is thought to be sufficient to prevent dehydration which might otherwise result from vomiting and diarrhea. Later the fluid intake is gauged by the approximate amount of water lost in vomiting and diarrhea, and by the output of urine. Most of the fluid is given intravenously or

* No antidote was given to the 34 patients, all of whom were treated prior to the publication of Rosenthal's[20] work on the use of sodium formaldehyde sulphoxylate. Our experiences with this antidote have been reported elsewhere.[21]

subcutaneously early in the intoxication, even though there is little or no vomiting, because of the frequent occurrence of gangrenous lesions of the stomach and upper bowel in these patients.[18] The most convenient method of supplying fluid is the employment of a slow intravenous drip.

3. *The Use of Salt and Glucose.* These are given to prevent hypochloremia and acidosis, and to mitigate protein destruction. They are usually employed together, equal parts of 10 per cent glucose and normal saline being used in the intravenous drip.

4. *The Administration of Alkalis.* If the patient is not vomiting, he is given four grams of sodium citrate every three or four hours. If he desires fluid, he may take small amounts of imperial drink, well-sweetened fruit drinks, or water.

This régime is varied according to the exigencies of each case. If toxic manifestations appear, therapy is regulated according to the symptoms and their severity. The important symptoms in severe intoxications are shock, vomiting, abdominal distention, diarrhea, oliguria and anuria, and stomatitis. Vitiated physiologic processes are indicated by elevation of the non-protein nitrogen of the blood, by decrease of blood chloride, and diminution of plasma bicarbonate.

Shock. An initial hypodermic dose of morphine is given to allay pain, which is probably partly responsible for shock. An infusion of glucose in salt solution is begun, caffeine sodium benzoate is given intravenously and adrenalin intramuscularly. After the institution of these measures, the stomach is washed out. We consider it important that lavage be delayed until measures have been taken to combat shock, since attempts at immediate lavage may aggravate the collapse already present; the patient may even die during the attempted lavage procedure.

If shock is not relieved by these measures, a transfusion (500 c.c. of citrated blood) is given as soon as possible, 0.3 c.c. of adrenalin is injected intramuscularly every 20 to 30 minutes, and 0.5 gram of caffeine sodium benzoate is given intravenously every three hours.

Vomiting, Distention, Diarrhea. Continued vomiting usually co-exists with tympanites. Nothing at all is given by mouth; the stomach is washed out gently with normal saline, the tube left in and aspirated at intervals. Extra fluid and salt are supplied intravenously to replace that removed by aspiration. A rectal tube is inserted and a heat tent placed over the abdomen. For protracted distention hypertonic salt solution is given intravenously, as recommended by Ochsner and Gage[22] in the therapy of adynamic ileus (5 c.c. of distilled water and 20 c.c. of concentrated Hartmann's solution).

Diarrhea is seldom as troublesome as vomiting, usually subsiding spontaneously after a few days. We use colonic irrigations of warm normal saline and give opium and bismuth subnitrate by mouth if diarrhea persists.

Oliguria and Anuria. It is difficult to state how much water and salt it is advisable to give a patient who is secreting no urine or very small amounts.

It is possible that mechanical blockage of the renal tubules by necrotic, swollen epithelium may be concerned in the mechanism of anuria in mercury poisoning [23]; a large intake of fluid, which favors increased glomerular filtration, might tend to "force the renal block." [24] The work of Barry, Shafton and Ivy [25] on nephrectomized dogs also indicates that the parenteral administration of fluid and salt might prolong the lives of anuric patients until such a time as secretion of urine will be reëstablished. It is, however, dangerous to give large amounts of water and salt to patients with anuria. Although edema is not usually a part of the clinical picture of bichloride poisoning,[26] it can be constantly produced if large amounts of water, together with salt, are given to these patients.[27] While moderate subcutaneous edema may not be harmful, the continued forcing of fluid and salt may result in rapidly developing massive pleural, pericardial and peritoneal effusions, and the patient may die suddenly of acute heart failure. We have seen this happen to two patients, one of whom was under the care of one of us (E. H.). At present we feel that in the absence of edema, it is safe to give 3000 c.c. of water daily, above the amount lost via the gastrointestinal tract, approximately the amount required by a normal individual (including the water derived from food),[28] and to push the administration of salt as long as the blood chloride is below normal. When any edema at all appears, it seems advisable to reduce the fluid intake, and to give very little saline, if any at all; it is probably unsafe to give more than 1500 to 2000 c.c. of fluid in excess of that lost in stools and vomitus. [Approximately 1800 c.c. of water are lost each day via the skin and lungs in a normal person.[28]]

Diuretics have been used in all patients with anuria or severe oliguria. Fifty c.c. of 50 per cent glucose are given intravenously twice a day, and 0.5 gram of theophylline ethylene diamine * intravenously daily for three or four days. On occasion, we have tried potassium chloride by mouth (6 to 8 grams daily) and intravenously (300 c.c. of 1 per cent solution). While no apparent deleterious effects have followed the use of any of these substances, we have not observed striking diuresis following the administration of any of them.

Hypochloremia. If the blood chloride remains below normal, in spite of the administration of normal saline, 2 per cent sodium chloride solution is substituted. Marked reduction of blood chloride was not encountered in any patients reported in this series.

Acidosis. The carbon dioxide combining power of the blood plasma is determined daily on all severely toxic patients. When, on the usual therapeutic régime, this falls below 40 volumes per cent, alkalis or buffer salts are given intravenously. We have used Hartmann's solution, molar sodium lactate (Hartmann), Fischer's solution, and sodium bicarbonate (2.5 to 5 per cent solution). At present we are using sodium bicarbonate in 5 per cent solution, when the indication for intravenous alkali therapy is present.† All

* There is evidence that this drug produces diuresis by increasing glomerular filtration.[29]

† Experience with the intravenous use of sodium bicarbonate in acidosis indicates that 500 c.c. of 5 per cent solution usually increase the CO_2 combining power about eight volumes per cent.

of these preparations, because of their sodium content, may aggravate preexisting edema, and should be used very cautiously in its presence. We believe that the presence of edema contraindicates the use of Fischer's solution; in one patient, a marked increase of edema, with hydrothorax and ascites, followed its use.

Other Symptoms. Mouth washes containing sodium perborate or potassium permanganate are used for stomatitis. Morphine and phenobarbital sodium are given freely when sedation is required. Calcium gluconate (1 gram) is given intravenously for muscular twitchings in patients with uremia; the twitchings are probably due to hypocalcemia.[30] Transfusions are given if much bleeding from stomach or bowel occurs.

Results of Therapy

Thirty-four patients reputedly poisoned with mercuric chloride were treated according to this method; there were three deaths, a mortality of approximately 9 per cent. Since in the past, the mortality following bichloride ingestion has been about 25 per cent in Charity Hospital,[18] it might appear at first glance that the newer therapy is strikingly superior to the methods formerly in use. A close analysis of the cases, however, shows that there is no occasion for enthusiasm.

Of the 34 patients, only 10, less than a third, developed any signs at all of mercury poisoning, whereas, in the past, about half of the patients had manifested definite signs attributable to the toxic effects of mercury.[18] Since so many variable factors, difficult to ascertain reliably, determine whether toxic symptoms appear at all, and since we see no reason why this method of therapy should prevent the appearance of all the manifestations of mercury poisoning, we must attribute the lower incidence of "toxic" cases in this series, not to any effect of treatment, but to the fact that in a larger proportion of these patients, the amount of mercury absorbed was not sufficient to be poisonous. The lower mortality, therefore, does not necessarily signify improved therapeutic results.

The mortality in the 10 "toxic" cases is 30 per cent, which is lower than that in "toxic" cases treated in the past by other methods (50 per cent),[18] but not significantly so, in view of the small number of cases in the present series. In five of the 10 cases, the intoxication was mild or only moderately severe, and it seems likely that these patients would have recovered without any special therapy, although it is of course possible that the therapy employed mitigated the severity of the intoxication. Any claim for merit of the therapy employed must be based upon results in the five cases in which the intoxication was markedly severe. Had all of these patients, or four of the five, recovered, this would have constituted strong evidence of merit of the treatment,* but three of the patients died, one early in shock, two of uremia. It is thus clear that this series offers no statistical evidence

* The mortality of severe mercury poisoning in Charity Hospital has been almost 90 per cent.[18]

to prove the superiority of this method of therapy. The recovery of one patient in whom the prognosis, from an appraisal of the early signs, seemed very unfavorable, is the only indication that therapy directed towards the combatting disturbed physiologic processes may occasionally be life-saving in severe mercury poisoning.

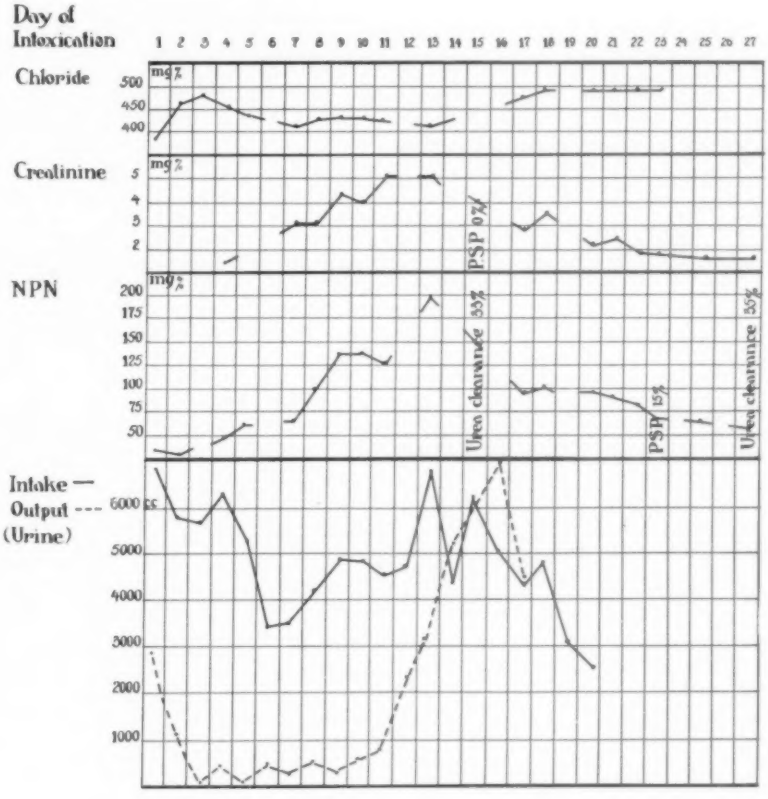

CHART I

CASE I

A white female, aged 23, took 10 bichloride tablets (73 grains) dissolved in a glass of water; she had eaten a sandwich and drunk some beer a short time before ingestion of the poison. Vomiting occurred in less than five minutes; gastric lavage was done a half hour later. Vomiting continued, and bloody diarrhea appeared in about two hours.

After the usual emergency measures, glucose and saline were given continuously by intravenous drip. During the first 24 hours, she received a total of 6800 c.c. of fluid, of which only 1800 c.c. were given by mouth. During this period the output of urine was 2800 c.c.

Diarrhea lasted only two days; vomiting persisted for a week. Abdominal distention was marked. Stomatitis appeared on the third day. On the sixth day, a necrotizing lesion of the vagina was observed. Marked oliguria developed on the third day and persisted for eight days, the daily output varying from 150 to 500 c.c.

The urine passed during this period was of very low specific gravity (1.000 to 1.004), and contained only small amounts of albumin and a few casts. (Chart 1.)

The non-protein nitrogen of the blood rose gradually; on the tenth day of the intoxication, it had reached 133 mg. per cent. No significant diminution of blood chloride occurred. Edema of the face and legs appeared on the fourth day; at this point, part of the chloride intake was given as potassium chloride. What was considered to be adequate amounts of fluid (in reality, perhaps too much) was supplied by vein and hypodermoclysis, and by mouth after vomiting and tympanites had subsided.

Fifty c.c. of 50 per cent glucose were given intravenously every day during the period of oliguria; twice she received 0.5 gram of metaphyllin intravenously. Edema of the face and extremities increased, and signs of ascites appeared. On the eleventh day, while an intravenous drip was running, she experienced a sudden attack of dyspnea; after an injection of morphine and discontinuance of the drip, the attack subsided promptly.

On the twelfth day, there was a sharp rise in the output of urine; from this day diuresis was maintained, edema diminished, and recovery was rapid. Clinical improvement as evidenced by copious diuresis preceded the fall of the N.P.N. level; on the thirteenth day, when 3200 c.c. of urine were voided, the N.P.N. reached its highest level, 190 mg. per cent. On the fifteenth day, when 5000 c.c. of urine were passed, there was no phthalein excretion after two hours, and the N.P.N. was 150 mg. per cent.

The patient was discharged 34 days after ingestion of the poison, apparently in good health.

Most of the factors that determine the prognosis in mercury poisoning indicated an unfavorable outlook for this patient, in spite of the early vomiting and the fact that her stomach was not empty. The dose was more than sufficient to kill, the drug was taken in solution, and severe toxic manifestations appeared early.[18] The long duration of oliguria and the high levels that the non-protein nitrogen and creatinine reached also bespoke a poor prognosis.[18] It may be significant that the non-protein nitrogen of the blood rose very slowly in the presence of such marked diminution of urinary output, and that there were no uremic manifestations.

Summary

1. Thirty-four patients, who ingested bichloride of mercury, have been treated by a method designed chiefly to prevent and combat the physiologic disturbances occasioned by the presence of mercury in the body. The method is almost identical with the one proposed recently by Peters, Eisenman, and Kydd.

2. Only 10 of the patients developed any signs of mercury poisoning. In five, the intoxication was mild or of moderate severity; in the remaining five it was very severe.

3. Three patients died, a mortality of approximately 9 per cent. Although in the past, the mortality of mercury poisoning in Charity Hospital has been about 25 per cent, a study of the individual cases in the present series indicates that the lower mortality is not necessarily due to the changed method of therapy.

REFERENCES

1. Lambert, S. W., and Patterson, H. S.: Poisoning by mercuric chloride and its treatment, Arch. Int. Med., 1915, xvi, 865–879.
2. Wilms, J. H.: Calcium sulphide as the chemical and clinical antidote for mercuric chloride poisoning, Jr. Lab. and Clin. Med., 1917, ii, 445–458.
3. Carter, T. A.: Mercuric chloride poisoning, Chicago Med. Rec., 1914, xxxvi, 444–460.
4. Fantus, B., and Hyatt, E. G.: Antidotes in mercuric chloride poisoning, Jr. Lab. and Clin. Med., 1917, ii, 813–818.
5. Zeigler, W. H.: A study of the efficacy of certain antidotes in the treatment of acute bichloride of mercury poisoning, Jr. Lab. and Clin. Med., 1925, x, 259–268.
6. Sabbatani, L.: Biochem. Centralbl., 1906, 502. (Quoted by Wilms.[2])
7. Dennie, C. C., and McBride, W. L.: Treatment of arsphenamine dermatitis and certain other metallic poisonings, Arch. Dermat. and Syph., 1923, vii, 63–76.
8. Weiss, H. B.: Methods of treatment of mercuric chloride poisoning, Jr. Am. Med. Assoc., 1917, lxviii, 1618–1620. Mercuric chloride poisoning, Arch. Int. Med., 1924, xxxiii, 224–229.
9. MacNider, W. deB.: Study of acute mercuric intoxication in dog, Jr. Exper. Med., 1918, xxvii, 519–538.
10. Fischer, M.: Edema and nephritis, 1921, 3rd Ed., John Wiley and Sons, New York, p. 735.
11. Lewis, D. S., and Rivers, T. M.: Chemical studies on a case of bichloride poisoning, Johns Hopkins Hosp. Bull., 1916, xxvii, 193–201.
12. Campbell, W. R.: Acute mercuric chloride nephrosis, Arch. Int. Med., 1917, xx, 919–930.
13. Hayman, J. M., Jr., and Priestley, J. T.: Importance of diuresis in treatment of certain cases of mercuric chloride poisoning, Am. Jr. Med. Sci., 1928, clxxvi, 510–516.
14. Peters, J. P., and Van Slyke, D. D.: Quantitative clinical chemistry, Vol. 1, 1931, Williams and Wilkins, Baltimore, p. 1156.
15. Lemierre, A., Laudat, M., and Laporte, A.: Deux cas de néphrite mercurielle traités par la choruration, Presse méd., 1932, xl, 1637–1640.
16. Haskell, C. C., Carder, J. R., and Coffindaffer, R. S.: Value of forcing fluid in treatment of mercuric chloride poisoning, Jr. Am. Med. Assoc., 1923, lxxxi, 448–450.
17. Rosenbloom, J.: Studies in a case of acute bichloride of mercury poisoning, Am. Jr. Med. Sci., 1919, clvii, 348–356.
18. Hull, E., and Monte, L. A.: Bichloride of mercury poisoning; a statistical study of 302 cases, South. Med. Jr., 1934, xxvii, 918–924.
19. Peters, J. P., Eisenman, A. J., and Kydd, D. M.: Mercury poisoning, Am. Jr. Med. Sci., 1933, clxxxv, 149–171.
20. Rosenthal, S. M.: Antidote for acute mercury poisoning, Jr. Am. Med. Assoc., 1934, cii, 1273–1276.
21. Monte, L. A., and Hull, E.: Bichloride of mercury poisoning; sodium formaldehyde sulphoxylate as antidote, South. Med. Jr., 1934, xxvii, 988–990.
22. Ochsner, A. E., and Gage, I. M.: Adynamic ileus, Am. Jr. Surg., 1933, xx, 378–404.
23. Fishberg, A. M.: Hypertension and nephritis, 1931, Lea and Febiger, Philadelphia, p. 280.
24. Volhard, F.: Mohr and Staehelin's Handbuch der inneren Medizin, 1918, iii, 1554, J. Springer, Berlin.
25. Barry, F. S., Shafton, A. L., and Ivy, A. C.: Experimental edema in nephrectomized dogs; rôle of water and chlorides, Arch. Int. Med., 1933, li, 200–206.
26. Fishberg, A. M.: See reference 23, p. 282.
27. Hull, E., and Monte, L. A.: Unpublished studies.
28. Howell, W. H.: Text-book of physiology, 12th Ed., 1933, W. B. Saunders, Philadelphia, p. 911.
29. Herrmann, G., Stone, C. T., Schwab, E. H., and Bondurant, W. W.: Diuresis in patients with congestive heart failure, Jr. Am. Med. Assoc., 1932, xcix, 1647–1652.
30. Fishberg, A. M.: See reference 23, p. 137.

"EVENTRATION" OF THE RIGHT DIAPHRAGM: REPORT OF A CASE WITH REVIEW OF THE LITERATURE, CHIEFLY FROM THE STANDPOINT OF ETIOLOGY AND DIAGNOSIS *

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THE condition commonly called "eventration" of the diaphragm is understood to mean an abnormally high position of one-half of the phrenic leaf, caused not simply by displacement, but by aplasia (congenital), or atrophy (acquired) of the muscle fibers of the half of the diaphragm. As a result, the abdominal viscera are displaced upward into the thoracic cavity. The unduly expanded leaflet is intact and its position is permanent.

This abnormality has passed into the literature under more names than any other lesion of the diaphragm. The names, "elevation," "relaxation," "high position," "insufficiency" and "dilatation" have been used to designate this pathological state. While eventration is a gross misnomer, since it suggests the displacement of the viscera out of the abdomen, it has received by custom a connotation which is specific for this condition of the diaphragm (Bayne-Jones).

A brief review of the development of the diaphragm [1] is warranted in order better to understand this abnormality. The anterior end of the celom containing the heart is shut off by a partition which forms at about the sixth week of intrauterine life; and at a slightly later date, the two pleural sacs are separated from the peritoneal cavity by the completion of the diaphragm. The greater part of the latter is formed from the septum transversum, which is ventral in situation, while the dorsolateral portions are derived from the pleuroperitoneal membranes which close the communicating ducts between the two cavities on the right and left sides.

The musculature of the diaphragm is stated to be developed from two muscle masses derived from the fourth cervical myotome.[1] These grow into the developing diaphragm, while the septum transversum is still in the cervical region. Later the diaphragm migrates caudally to reach the proper place.

In eventration the cupola forms a thin sac with normal attachments, but projecting into the thorax to reach a high level. It seems probable, therefore, that neither failure of migration nor a failure in the union of the component parts is responsible for the condition, but that it is due to failure of development of the musculature on one side. As a result of this, the muscle sheet is almost entirely replaced by a thin membrane, which yields very readily to abdominal pressure.[1]

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However, there have been varied opinions as to the etiology of eventration ever since its discovery (1784). Thoma [2] believed that the condition was secondary to congenital malformation of the lung on the affected side, and that the diaphragm rose to fill the space in the pleural cavity. Doering,[3] on the other hand, favored the view of a primary deficiency of half of the diaphragm. The symmetrical condition of the thorax in eventration he employed as an argument in favor of his view. Clinical experience in chronic diseases of the chest associated with elevation of the diaphragm due to traction from adhesions demonstrates that malformation and asymmetry of the chest wall are usually the result. Falkenstein [4] has shown that idiopathic degeneration of the diaphragm frequently occurs, the lesion being a fatty degeneration of the muscle. Aronson [5] enumerates many diseases that may affect the motor columns of the cervical cord, and thus give rise to an acquired eventration. He also lists neuritis of the phrenic nerve as a possible cause. Christian [6] strongly believes that the cause of eventration is congenital. That it is frequently seen in infants; that there is no history of trauma; and that the affected lung is not compressed, are arguments he employs in favor of his view.

At autopsy the lung on the affected side is usually small and hypoplastic, but atelectasis has not been observed. The eventrated diaphragm is a thin translucent membrane, containing a few muscle fibers and smoothly covered by pleura and peritoneum. The phrenic nerve is usually reduced in size, but otherwise normal.

The first authentic case of eventration is that of Petit [7] in 1790. He himself did not employ the term "eventration" but considered the condition a peculiar variety of diaphragmatic hernia. Cruveilhier [8] in 1849 was the one to coin the name eventration and elucidate the essential differences between hernia and eventration. Bamberger [9] in 1913 compiled 31 cases. Bayne-Jones [10] in 1916 collected 41 cases. Gläser [11] in 1901 was the first to diagnose this condition during life. Hirsch [12] in 1901 was the first to make a roentgenological diagnosis. He diagnosed hernia of the diaphragm and eventration was found at autopsy. There were over 100 cases of eventration reported in the literature up to 1926. The greater number of instances of this rare anomaly occur on the left side. Korns [13] in 1921 critically reviewed the literature and found only 18 proved cases of left eventration and 41 which, though not proved, seemed reasonably certain, thus making a total of 59 cases. The same author listed only the following five cases of eventration of the right diaphragm: Two of Eppinger's in 1911 which were substantiated by necropsy; a case by Glässner in 1916; a fourth case, described in 1916 by Bayne-Jones, who made the diagnosis purely by physical examination, subsequent roentgenological examination and laparotomy confirming his clinical impression; and Aronson's case reported in 1918, which Korns considers not completely proved because of the author's vague description of the findings. If genuine, it is the fifth case. Korns' own case makes a sixth. He diagnosed his case by roentgen-ray and physi-

cal findings, based on the physiology of the intercostal muscles and the diaphragm. He concluded that of these six cases, in four the diagnosis may be considered proved, while in two it is not proved but reasonably certain.

Golob [14] in 1926 reported a case of right eventration, proved at operation. Fatou and Prévost [15] described a case of right eventration in 1928, thus raising the number of cases to eight. Morris' [16] case in 1929 of right sided eventration with transposition of the stomach, colon and liver, diagnosed by the roentgen-ray is the ninth. Our case of right eventration is the tenth to be described.

Eventration of the diaphragm should not be looked upon as just a rare curiosity to be relegated to the pathological museum. Recognition of this abnormality is important in order to prevent confusion with other conditions situated above and below the diaphragm. Without the assistance of the roentgen-ray, eventration has been mistaken for pleural effusion, encysted empyema, and abscess of the lung. Exploratory thoracenteses have been performed. The results of this procedure may be very tragic. The discovery of eventration in women of the child-bearing age is very important for it may turn out to be a menace to life. In one instance [17] where a complication precipitated labor before a planned Caesarean section was undertaken, the patient died because of a ruptured diaphragm. In our case forceps had to be applied in the second stage of labor, because her "bearing down" was of no avail. At that time, however, it was not known that she had such an anomaly of the diaphragm.

This anomaly is also important because of the readiness with which it may be confused with diaphragmatic hernia. The latter condition often lends itself to surgical repair, but in eventration operation is useless. The differentiation, however, between these two conditions may be impossible even after resorting to all available safe methods of investigation, short of an exploratory laparotomy.

There are no distinctive symptoms of eventration of the diaphragm. In most instances it is asymptomatic, since both the thoracic and abdominal viscera accommodate themselves to this congenital defect. However, there may be some cardiac, pulmonary, or gastric symptoms: palpitation, slight dyspnea, "gas" pains after meals, asthmatic attacks or substernal pain. Cyanosis and weakness have been observed as well as nausea and vomiting.

The condition may be suspected on physical examination, but in most instances it has been discovered as the result of roentgen-ray examination or at autopsy. The usual findings are absence of Litten's shadow, dullness, and absence of breath sounds on the affected side. The chest is symmetrical, and the inspiratory expansion of the two sides of the chest, with the exception of the costal margins, is the same. In right sided eventration the position of the heart is not changed to as appreciable a degree as it frequently is in left eventration. Tympanitic sounds may be elicited over the affected side of the thorax, depending greatly on how much food or gas

there is in the viscera during the examination. Peristaltic sounds in the chest are very significant, but Lord [18] cautions against this finding. He states that normally, peristaltic sounds may be heard on the left side as high as the third rib in front and lower third of scapula behind, and at a somewhat lower level on the right side. These peristaltic sounds are much louder on the left than on the right.

However, there is a physical sign, which, according to Korns [13] and Lord,[18] is the most valuable and the least used in the diagnosis of eventration of the diaphragm. It is the Hoover sign—an exaggerated inspiratory divergence from the median line of the entire costal margin on the affected side. It is elicited with the patient in the recumbent position. This sign is based on the work of Hoover [19] on the physiology of the diaphragm and of the intercostal muscles.

The diaphragm and the intercostal muscles are antagonists. The former increases the longitudinal diameter, while the latter increase the transverse and the anteroposterior diameters of the thorax. The excursion of the abdominal wall is a measure of the excursion of the diaphragm. The lower six intercostal muscles and the diaphragm are also antagonists in controlling the movements of the costal border. Unopposed by the phrenic action, the intercostal muscles will cause the entire costal margin to move away from the median line, and unopposed by the intercostals the diaphragm will draw the entire costal margin toward the median line. Hence, the movement of the costal margin during normal inspiration is the resultant of the opposed actions of the intercostal muscles and the diaphragm.[19]

The extent to which the diaphragm is able to oppose the intercostal muscles depends upon the arch, and the more nearly the curve approaches a plane, the greater is its mechanical advantage.[18] If the diaphragm is at a mechanical disadvantage by upward displacement, or if its muscles are injured, the pull of the intercostal muscles is more effective. The result is a distinct inspiratory widening of the subcostal angle, caused by the exaggerated inspiratory divergence from the median line of the entire costal margin, from the xyphoid to the post-axillary line.

Korns [13] urges the use of palpation besides inspection in eliciting this sign. The palpation should be applied to the extreme ends of the ribs of the costal margin, and not to the arcs of the ribs. The movement of the latter is upward and outward in a "bucket-handle" fashion in response to normal activation of the intercostal muscles. Thus in obese patients palpation, we think, may elicit this outward excursion of the costal margin, while inspection may not. Such was our experience with our case.

The evidence of activation or want of activation of half of the phrenic leaf is especially of value in the differential diagnosis between hernia and eventration [13] of the diaphragm. In hernia, Hoover's sign is not observed, unless in a very marked herniation with a very extensive aperture, which is exceptional. If there should be any asymmetry in movement, it occurs as a lessened outward movement on the affected side, due either to a flattening of

the diaphragm, or to its acquisition of a high insertion from the formation of pleural synechiae between it and the thoracic wall.

Eventration of the diaphragm must, naturally, also be differentiated from such conditions as pneumothorax, subphrenic abscess, large basal cavities, and paralysis of the diaphragm.

In most instances eventration is discovered as a result of roentgenological study, and such studies constitute the most reliable laboratory procedure we have. Walton [20] enumerates the following diagnostic roentgenological signs:

(1) *High position* of the affected diaphragm is present, and it may be as high as the second interspace.

(2) *Regular* contour of the arched line is a sign stressed very much. There is always present the typical curved line of the dome of the diaphragm. In hernia, the contour of the arch is somewhat irregular and usually nodular,[21] and when an opaque meal is given, marked derangement of the arch by the new shadow is seen. However, this finding does not absolutely differentiate eventration from a hernia in which the contour of a dilated stomach or colon may give a similar regular arched line.

(3) *Excursion* of the affected half of the phrenic leaf is usually present, but very much limited. Under the fluorescent screen, the normal side exhibits normal excursion, and there is no evidence of exaggeration to compensate for the affected side. When the patient is instructed to breathe deeply, the abnormally elevated diaphragm will be seen to move slightly up and down to the extent of probably a few centimeters only.

(4) *Paradoxical movement* of the affected side of the diaphragm as a test has no great significance. Assmann [21] comments on the unreliability of this sign. For a time this was regarded as a distinguishing sign, but recent observers agree that respiratory movement may be normal, diminished, absent, or reversed in either eventration or hernia.[22]

(5) Inspiratory excursion of the mediastinum toward the sound side has been observed three times according to Korns.[13] This phenomenon is due to the development of a relatively greater degree of negative pressure in the sound side because of the presence of diaphragmatic contraction on that side. Similar phenomena may be observed in unilateral paralysis of the phrenic nerve. The reverse is usually seen in bronchial obstruction, where the excursion of the mediastinum is toward the affected side. While this sign should be looked for in suspected eventration it is very often absent, and when present, its value in differential diagnosis is questionable.[20]

(6) Displacement of the heart is frequently seen in left sided eventration thus giving rise to dextrocardia. Whenever the latter is diagnosed, the condition of the left diaphragm should be investigated. In right sided eventration the heart is usually not appreciably displaced. It seems that the displacement of the heart in right sided eventration depends upon what organs are prolapsed into the thorax. When the liver is high up, the heart is pushed over to a much lesser degree than when the big bowel is high in

the thorax. In our case, a barium enema produced quite a bit of distress, because the distention of the colon displaced the mediastinal structures still more to the left.

(7) *Pneumoperitoneum* is classified among the diagnostic signs. Walton,[20] after enumerating the roentgenological findings discussed above, concludes that the only pathognomonic finding in eventration of the diaphragm is a distinguishable separation of the arched line of the dome of the diaphragm from the viscera below, accomplished by injecting air into the peritoneal cavity. Lord [18] questions whether this procedure is justified, since in the presence of a diaphragmatic hernia, pneumoperitoneum may entail some risk. The absence of a sac in the majority of cases of diaphragmatic hernia, and the imperfect closure of the defect in the diaphragm by the hernia, make it likely that the introduction of gas into the peritoneal cavity will cause a pneumothorax. He also cites the case of Schlect and Wels who used this method in a congenital diaphragmatic hernia. Three weeks later their patient developed severe abdominal pain, followed by collapse. The operation revealed perforation and gangrene of the greater curvature of the stomach. The possibility that the pneumoperitoneum, by displacing the stomach and interfering with its blood supply, might have been responsible, could not be excluded by them. Lord [18] feels that if the symptoms are severe and more suggestive of a hernia than of eventration, it is better to do an exploratory operation and repair the hernia if found and feasible, than to subject the patient to the risk of a pneumoperitoneum. This procedure was not employed in our case.

(8) Lateral roentgen views of the chest are of diagnostic help in abnormalities of the diaphragm. Their employment is often mentioned in the British literature [1, 16] as a means of differentiating eventration from hernia of the diaphragm. In the former, the lateral view shows the smooth curved contour of the elevated dome. It is especially recommended that an opaque meal be given, and the film taken with the patient lying on a side. In case of hernia this position will facilitate the passage of some of the barium into the pouch above the diaphragm.

Some part of the bowel was found displaced in all cases of right sided eventration studied roentgenologically with the opaque meal. Thus in Bayne-Jones' [10] case the transverse colon was displaced, looped, and doubled on itself in the right upper quadrant. The liver, however, was found high up under the ribs, and covered by the diaphragm. In Aronson's [5] case the dilated colon was in the right chest above the liver and covered by the diaphragm. The proximal colon was anterior to the liver and under the right diaphragm in the case described by Golob.[14] Morris' [16] case had the stomach under the right diaphragm. Our case, too, had bowel in the right thorax situated right under the diaphragm. Finding the displaced bowel in the right chest and under the elevated diaphragm, weakens the argument of those who assert that in congenital eventration it is the liver that is invariably found under the diaphragm.[15]

Measurements of changes in the intragastric pressure during respiration have been used by some to differentiate between hernia and eventration of the diaphragm. Hildebrand and Hess [23] used this method in their case and their diagnosis was confirmed by autopsy. They demonstrated an inspiratory rise and an expiratory fall in the intragastric pressure, which is the reverse of what should occur if the stomach had invaded the thorax through a hole in the diaphragm. The test, however, is not as valuable as was at first anticipated, for the intragastric pressure has been shown to vary normally with intercostal and abdominal types of respiration.

Most of the instances of eventration require no treatment. However, strenuous exercise should be prohibited. Pregnancy, if it occurs, should not be allowed to go on to labor, but should be terminated by abdominal section. Those who are overweight should aim to reduce. Should troublesome symptoms be present, surgical intervention may be considered. In Lerch's case, quoted by Lord, three plaits were taken in the diaphragm through an incision in the outer part of the rectus muscle. The patient improved and seven months after the operation she was entirely relieved of her pulmonary and gastric symptoms.

Case Report

M. L., Jewish, aged 27, married, primipara, housewife, was admitted to the obstetrical ward of the Mount Sinai Hospital (service of Dr. Chas. Newberger) on April 11, 1932.

Because of prolonged labor, exhaustion, and the patient's seeming inability to accomplish anything by "bearing down," forceps were applied and an episiotomy was done. She was sent back to the ward in good condition.

On the following day the intern on the service noticed that the patient was somewhat dyspneic and slightly cyanotic. She also complained of a slight cough. Eliciting definitely abnormal findings in the right chest, he fortunately became alarmed and ordered a bedside roentgenological examination.

The film was shown to us and we suggested that the condition might be an eventration of the diaphragm. The patient was transferred to our service (service of Dr. I. M. Trace) after her puerperium for a detailed study of her abnormality.

History. The pertinent statements in the history were as follows: Moderate shortness of breath upon exertion has been present ever since she can remember. A non-productive cough has bothered her since childhood. When she lies on her abdomen she becomes quite dyspneic, and often begins belching, which relieves her. Indefinite pains in the upper abdomen have been present all her life, which she ascribes to "gas." The pregnancy, however, did not aggravate her condition at all, being entirely symptomless.

There is no history of trauma or accident of any kind; her mother testified to that. During her entire childhood, she could never play as much, nor run as fast as her playmates, because of shortness of wind, and marked fatiguability. When one year of age, she had three attacks of pneumonia. Her mother could not furnish any more details as to this supposed pneumonia. In all probability, the findings on the side of the eventration were repeatedly taken for pneumonia.

Physical Examination. The patient was lying comfortably in bed, and was neither dyspneic nor cyanotic. The pulse was 80, regular, the temperature 99.2° F. rectally, and the blood pressure was 110 mm. of mercury systolic and 70 diastolic.

She was short, rather sthenic, and quite obese. The head and neck were not abnormal.

The chest was symmetrical and its antero-posterior diameter seemed enlarged. The inspiratory expansion of the two sides of the chest, except the costal margins, was the same. Litten's sign was not present on the right side.

There was dullness on the right side up to the second interspace anteriorly and up to the midscapular region posteriorly. (However, there were times in the following few years during which we observed the patient, when the dullness anteriorly gave way to a tympanitic note, and sometimes to a hyperresonant note. In view of

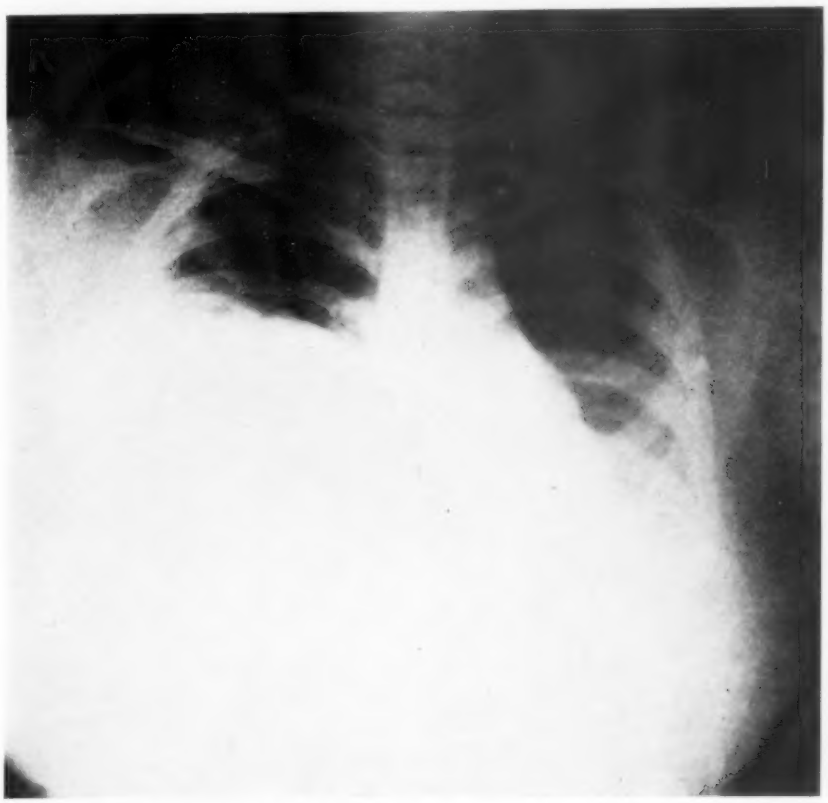

FIG. 1. Film taken at end of deep expiration. The curved line of the right phrenic leaf is at the lower border of the second rib anteriorly. The contour of the arched line is regular throughout its entire course. The trachea and heart are displaced somewhat to the left.

the roentgenological findings to be described later, the reason for these alterations in the percussion note is clear.) There were no compensatory changes on the left side. The heart dullness extended 11 cm. to the left of the mid-sternal line. No substernal dullness was elicited.

The breath sounds were very distant anteriorly, and were diminished posteriorly over the dull area; deep inspiration increased the breath sounds only slightly. Above this impaired area on the right the breath sounds were normal and were likewise normal over the left chest. There were no râles elicited at any time. Peristaltic

sounds in the right chest were heard while the patient was in the hospital, and several times since in the last few years. These sounds were heard anteriorly as high as the third interspace and about the midscapular region posteriorly. They were much louder anteriorly than posteriorly, and were best heard following an enema or a cathartic. At other times they were not loud, and one had to listen rather intently in order to hear them. The heart sounds were normal, and no murmurs or accentuations were present.

The Hoover Sign. With the patient in the recumbent position the contour of the

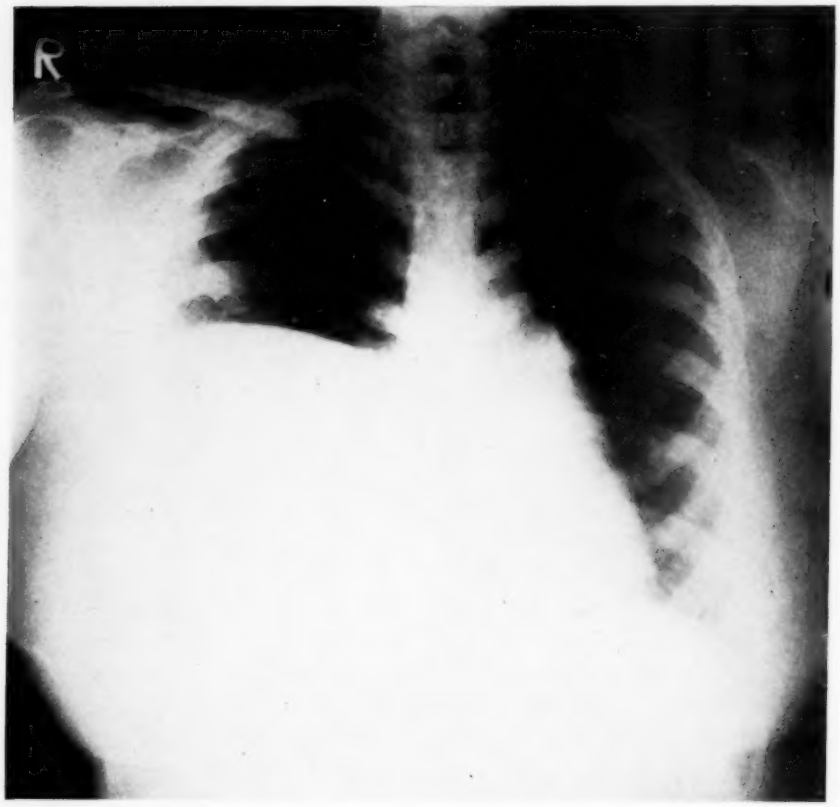

FIG. 2. Film taken at end of deep inspiration. The arched line of the right diaphragm is at the lower border of the third rib; thus it has moved one interspace downward during inspiration.

lower chest, the movement of the costal margins, and the excursion of the abdominal wall were studied.

Harrison's groove on the right side was much shallower than on the opposite side where it was quite marked, despite the patient's moderate obesity. This may have been the result of the action of the intercostal muscles on the right side unopposed by the inactivated diaphragm.

The excursion of the abdominal wall with the usual bulging in the epigastrium during inspiration was present on the left side, but absent on the right. This phenomenon is a measure of the excursion of the diaphragm and its absence means

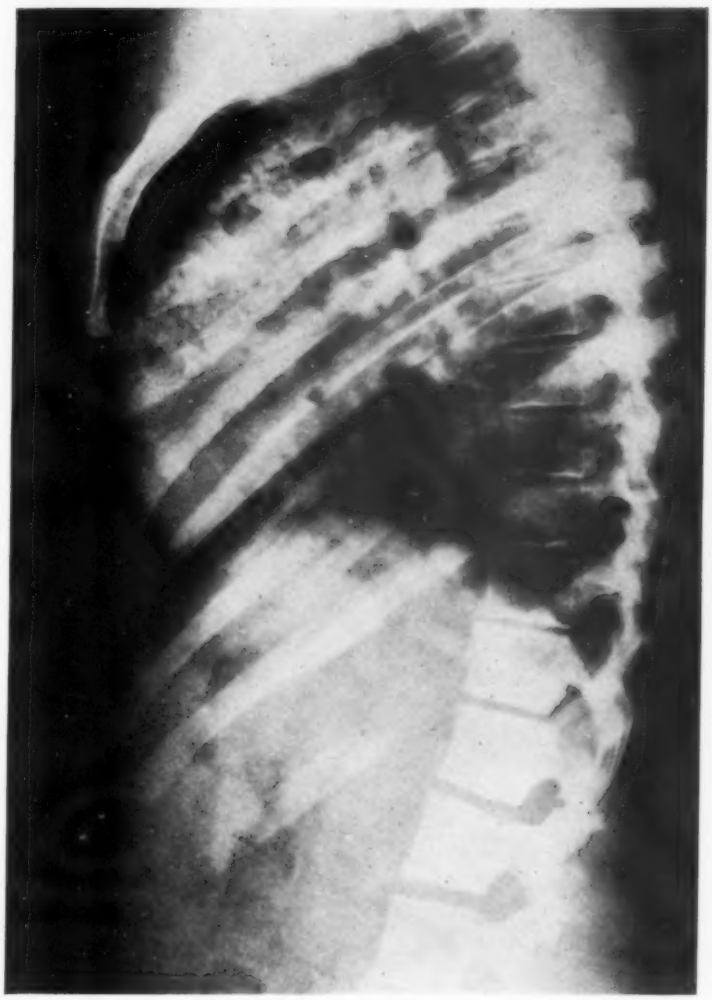

FIG. 3. Lateral view of thorax showing the dome of the right diaphragm high above and that of the left far below. Note that the contour of the eventrated diaphragm is regular throughout, and that bowel is situated under it.

that one leaf of the diaphragm is inactive. During deep inspiration there was a definite retraction of the right side of the epigastrium.

Inspection of the movement of the costal margin on the right side was not very convincing, as to its exaggerated inspiratory divergence from the median line, probably because of the patient's moderate obesity. However, it was certain that the right costal margin did not move in the same fashion or direction as the left one did, upward and outward.

Palpation of the right costal margin, however, showed definitely that there was an exaggerated inspiratory divergence from the median line. The finger tips were applied to the extreme ends of the ribs forming the costal margin, as suggested by Korns.[13] Thus the Hoover sign was positive in our case.

The abdomen was fairly obese; the liver, spleen, and kidneys were not felt. Percussion of the abdomen revealed dullness of the entire right side. The left side showed a moderately tympanitic note. (This finding has never varied.) Peristaltic sounds were few and always limited to the left side. There was no tenderness.

Laboratory Findings. The urine was normal. The blood showed a slight degree of hypochromic anemia. The Wassermann and Kahn tests were negative. The electrocardiogram was essentially normal.

Roentgenologic Examination. The film taken at the bedside, which suggested to us eventration of the diaphragm, showed the typical curved line of the right phrenic

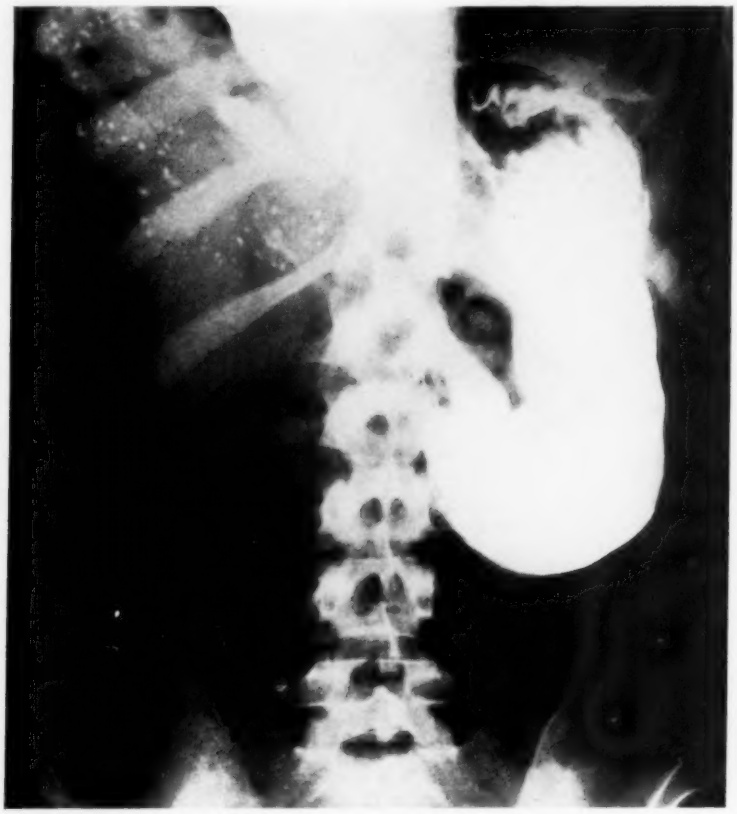

FIG. 4. Film taken immediately after a barium meal. The stomach is in its normal position. The duodenum is not seen, but when studied under the fluorescent screen it was normally situated and filled out completely. The barium, after leaving the first few inches of the jejunum, shot up into right thorax, instead of turning to the left and downward, as it normally does. The liver and kidney can be discerned in their normal places, and the bowel seems to enter the right thorax anteriorly to the liver.

leaf at the lower border of the second rib anteriorly. The contour of the arched line was regular throughout its entire course. The trachea and the heart were somewhat displaced to the left. The left diaphragm was in its usual position.

Later, films were taken of the chest at the end of deep expiration and inspiration. The arched line at the end of the latter phase was at the level of the lower border of

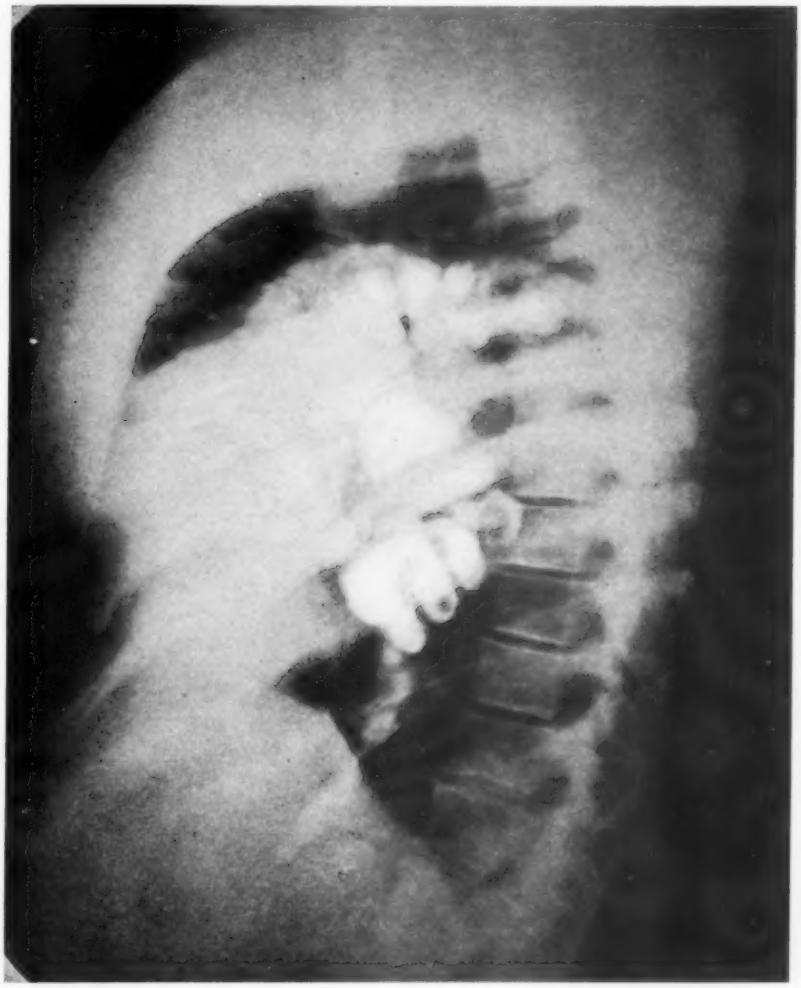

FIG. 5. Lateral view of thorax five hours after a barium meal. The latter is seen in the colon with the arched line of the right diaphragm above it. The contour of the curve is not deformed but it is as regular as before (see figure 3), thus speaking for eventration of the diaphragm.

the third rib anteriorly, thus showing how much the diaphragm had moved (figures 1 and 2). The other features were the same as in the first film.

Fluoroscopic examination confirmed the above findings. The right diaphragm was seen to move slightly downward upon deep inspiration and upward during deep expiration. Thus there was no paradoxical movement of the eventrated diaphragm in our case. In the lateral view one could visualize the regular arch of the right phrenic leaf and its slight excursion. The arch of the left diaphragm could also be seen, but at quite a distance below that of the right (figure 3).

Inspiratory excursion of the mediastinum was not present in our case. This sign was looked for on several occasions during the time that the patient was under ob-

servation, and we could never discover the slightest inspiratory deviation of the mediastinum.

The opaque meal showed that the esophagus and the stomach were in their normal positions. The stomach was of the fishhook type and without abnormalities. The duodenum was normally situated and filled out completely. The barium, after leaving the first few inches of the jejunum, shot up into the right thorax instead of turning to the left and downward as it normally does (figure 4). After five hours, all of the barium had left the stomach and was seen in the right chest. A lateral view

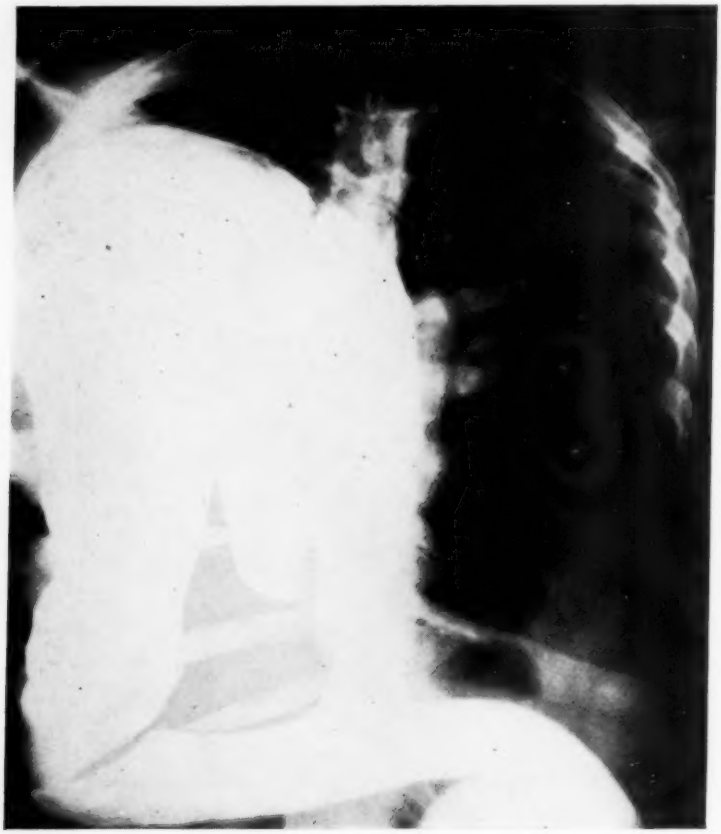

FIG. 6. An opaque enema showing that the cecum, ascending colon, hepatic flexure, and part of transverse colon are situated in the right thorax. Part of the cecum and first portion of the ascending colon are to the left and under the lower half of the sternum. The arch of the diaphragm is only faintly seen above the bowel.

at this time demonstrated the barium in the colon, with the arched line of the diaphragm above it. The contour of the latter was not deformed but remained as regular as before (figure 5). This lateral film was taken with the patient in the recumbent position. These findings speak against a hernia and for eventration of the diaphragm.

An opaque enema demonstrated that the cecum, appendix, ascending colon, hepatic flexure, and part of the transverse colon were situated in the right thorax, above the twelfth dorsal vertebra. The cecum and first part of the ascending colon were a little to the left of the midline and extending to the left side, thus displacing the

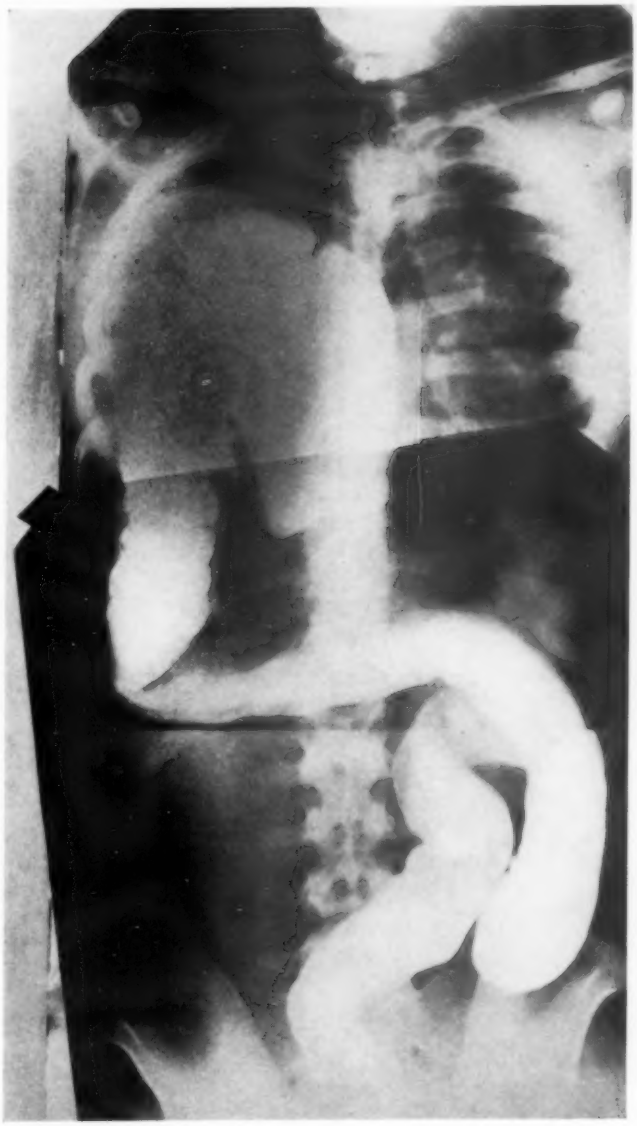

FIG. 7. A composite picture after an opaque enema showing the entire course of the large bowel. Note the marked displacement of the trachea and heart.

trachea and the heart to a still greater degree (figures 6 and 7). When the bowel was distended by the opaque enema, the patient complained of dyspnea, palpitation, and discomfort. She also became slightly cyanotic. It is entirely possible that the symptoms that aroused the curiosity of the intern in the obstetrical ward were due to the morning enema.

The liver and kidneys were seen to be in their normal position (figure 4). Pyelograms showed the kidney pelves to be normal.

Comment

The roentgen-ray findings showed that the intestinal tract between the first portion of the jejunum and the second portion of the transverse colon was extruded into the right thorax, and lay between the diaphragm above and the liver below. In this respect our case differs from the description of most of the reported cases in which it has been more usual to find the liver high up under the eventrated diaphragm.

Our patient has no bowel in the right side of the abdomen. Should she ever develop an attack of appendicitis, her symptoms would certainly be atypical and the method of surgical approach would have to be extraordinary indeed.

The patient has been under observation for the last few years. She feels quite well except for the slight discomforts mentioned above. Should she become pregnant again, an abdominal section will be strongly urged before labor sets in.

Conclusion

A case of right-side " eventration " is added to the literature, thus raising the number of reported cases to ten.

The diagnosis in this case was made because of the following findings:

(1) High position of the right diaphragm.

(2) Regular contour of the arched line as seen in the anteroposterior and lateral views.

(3) Definite, although limited, excursions of the elevated diaphragm.

(4) Roentgen-rays after an opaque meal and after a barium enema, with the patient in the recumbent position, showed that the arched line was the dome of the diaphragm, and not the outline of a distended bowel.

(5) Evidence of inactivation of the right half of the phrenic leaf (Hoover's sign).

The extruded bowel was situated between the right diaphragm above and the liver below, a finding unlike that in most cases reported.

REFERENCES

1. Wood, W. B., and Wood, F. G.: Congenital elevation of diaphragm, Lancet, 1931, ii, 392–397.
2. Thoma, R.: Vier Fälle von Hernia diaphragmatica, Arch. f. path. Anat., 1882, lxxxviii, 515–555.
3. Doering, H.: Über Eventratio diaphragmatica, Deutsch. Arch. f. klin. Med., 1902, lxxii, 407–414.
4. Falkenstein, quoted by Beck, C. H.: Eventration of diaphragm, Ann. Clin. Med., 1923, i, 362–371.
5. Aronson, E. A.: Hirschsprung's disease with eventration of right half of diaphragm, New York Med. Jr., 1918, cviii, 196.
6. Christian, H. A.: Eventration of the diaphragm, *in* Osler, W., and McCrae, T.: Modern medicine, Ed. 3, 1925, Lea and Febiger, Philadelphia, p. 344.
7. Petit, J. L.: Traite des maladies chirurgicales et des opérations qui leur conviennent, 1774, T. F. Didot, Paris.

8. CRUVEILHIER: Traite d'anatomie pathologique générale, 1849, Tome I, Baillière, Paris, pp. 614–617.
9. BAMBERGER: Ergebn. d. inn. Med. u. Kinderh., 1913, xii, 327.
10. BAYNE-JONES, S.: Eventration of the diaphragm with report of right sided eventration, Arch. Int. Med., 1916, xvii, 221.
11. GLÄSER, F.: Über Eventratio diaphragmatica, Deutsch. Arch. f. klin. Med., 1903, lxxviii, 370–379.
12. HIRSCH, C.: Zur klinischen Diagnose der Zwerchfell-hernie, München. med. Wchnschr., 1900, xlvii, 996–999.
13. KORNS, H. M.: Diagnosis of "eventration" of diaphragm, Arch. Int. Med., 1921, xxviii, 192.
14. GOLOB, M.: Right diaphragmatic eventration accompanied by cardiospasm as reflex of malignancy at cardia, Med. Jr. and Rec., 1926, cxxiv, 473–474.
15. FATOU, PRÉVOST, L., and PRÉVOST, F.: Un cas d'éventration diaphragmatique droite, Bull. et mém. Soc. med. d. hôp. d. Par., 1928, lii, 259–268.
16. MORRIS, H.: Eventration of the diaphragm, British Jr. Radiol., 1929, ii, 85.
17. BLACKFORD, L. M., and BOOTH, W. T.: Dextrocardia secondary to eventration of diaphragm; report of asymptomatic case, Jr. Am. Med. Assoc., 1932, xcviii, 883–885. (Quoting a case of Dr. R. A. Bartholomew.)
18. LORD, F. T.: Eventration of diaphragm, Arch. Surg., 1927, xiv, 316–329.
19. HOOVER, C. F.: Diagnostic significance of inspiratory movements of costal margins, Am. Jr. Med. Sci., 1920, clix, 663.
20. WALTON, H. J.: Eventration of diaphragm, Am. Jr. Roentgenol., 1924, xi, 420–426.
21. ASSMANN, H.: Quoted by KORNS, H. M.[13]
22. MOORE, A. B., and KIRKLIN, B. R.: Progress in roentgenologic diagnosis of diaphragmatic hernia, Jr. Am. Med. Assoc., 1930, xcv, 1966–1969.
23. HILDEBRAND, H., and HESS, O.: Zur Differential-diagnose zwischen Hernia diaphragmatica und Eventratio diaphragmatica, München. med. Wchnschr., 1905, lii, 745–748.

CASE REPORTS

INSTANT DEATH IN BACTERIAL ENDOCARDITIS: REPORT OF A CASE WITH MYCOTIC ULCERATION OF THE CONDUCTION SYSTEM *

By John G. Kidd, M. D., *Detroit, Michigan*

Sudden death, as it occurred in the present instance, is not the rule in subacute bacterial endocarditis. Such unexpected death contrasts sharply with the usual protracted course of this disease, so ably described by the late Dr. William Sidney Thayer in his remarkable monograph [1]:

> The disease is often distressingly chronic. Days and weeks and months pass by —every day with its morning of hope and its evening of depression. And the fatigue and the fever and the anorexia continue—moments, days, even weeks of apparent improvement and elation fatally dispelled by ever-recurring aggravations of first one, then another symptom. And slowly and surely the patient loses ground. The anemia increases. Evidences of myocardial insufficiency are added to the symptoms of chronic sepsis. The complexion assumes the peculiar, earthen greyish color, insisted on by Libman. With the advancing renal changes, the anorexia becomes more obstinate, and there is often nausea and vomiting. Edema of the face and dependent parts sets in. Profoundly enfeebled, with pale, grey, anxious face, puffy, transparent eyelids, inert, waxen, bulbous fingers, the patient is harassed by transient hallucinations of vision which he recognizes as hallucinations but cannot escape, by the dyspnea depending in part on the sepsis, in part on the anemia, in part on the nephritis, in part on the myocardial weakness, by the constantly recurring painful cutaneous or splenic emboli, by the persistent and unconquerable nausea. The least movement exhausts him; the nightly sweats weaken him; he is so tired! The very attentions of the nurse annoy him. And then, so often, as if to crown his ills, a sudden hemiplegia with flaccid arm and leg and drooping mouth and open eye. Finally, with wrinkled forehead and careworn face, he sinks into a troubled sleep and breathes his last—the victim of chronic sepsis, or myocardial weakness, or nephritis, or a terminal pneumonia, or cerebral embolism—or all.

In this paper photographs describe the anatomical lesions responsible for instantaneous death and the probable mechanism of death is discussed. Four similiar cases previously described in the literature are cited.

Report of Case

Summary: R. K. N., admitted August 18, 1932; died August 25, 1932. A boy of 18 complained of "rheumatism and heart trouble" recurring in attacks since the age of four. History, physical findings, and positive blood culture pointed to the diagnosis of subacute streptococcal endocarditis on the basis of old rheumatic heart disease. Remittent fever of 101 to 102 degrees daily was followed by unexpected instantaneous death on the eighth day after admission. At autopsy a large mycotic ulceration which

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From the Department of Medicine of the Henry Ford Hospital.

had almost perforated the ventricular septum was found occupying the site of the a-v node.

History. (Obtained from the patient and his mother.) At the age of four the patient had an attack of "rheumatism" which laid him up for two months. During this attack the elbows, wrists, fingers, knees and feet were swollen, tender and painful at one time or another. Just as the joint symptoms began to subside, extreme palpitation, dyspnea, and weakness were noted. These symptoms were attributed to heart disease by a physician at the time, and the patient stated that he had had them periodically since. Following this episode he was a delicate child, having frequent colds and attacks of sore throat until the age of nine, when he began to improve and entered school. For the next four years he was fairly well, and was able to do his work without interruption. At the age of 14 he won the high jumping championship of his class at school but while participating in a track meet he became chilled, a sore throat developed, and he spent the next several weeks in bed because of palpitation, dyspnea, and weakness. About a year later the patient missed a semester from school because of the same symptoms, and he was confined to bed in a hospital for 18 days during this period. Following this bout, however, he was fairly well until the onset of the present illness.

The immediate present illness began in March 1932, four months prior to admission to the hospital, when the patient was confined to bed for two weeks with an acute upper respiratory infection and fever which was diagnosed influenza. After this episode he was unable to attend school or to work because of weakness and dyspnea. One month before entry he again noted pain and swelling of the joints; mainly the left knee, left hip, and both ankles. These symptoms persisted until his entry, and during this month he lost five pounds in weight. On several occasions in the few weeks preceding admission, he had noted a precordial sensation of irregularity in his heart beat, and once, about two weeks prior to admission, while walking across a room, he stopped abruptly, grasped his precordium and exclaimed, "my heart stopped!" He became dizzy and felt faint, but the attack passed off a few minutes after he sat down. About 10 days prior to admission the patient and his mother noted the spontaneous appearance of several irregular purplish spots, resembling bruises, about the size of a silver quarter, near the left ankle.

Physical Examination. Temperature 99, pulse 100 and respirations 28. Weight 116 pounds—estimated ideal weight 156 pounds. The patient was a tall, emaciated boy of about 18 years who appeared sick and weak and uncomfortable. He had a subicteric pallor and was short of breath. There was no cough or cyanosis. Pulsation of the precordium and carotid vessels was striking and the whole bed oscillated with each heart beat. Petechiae were noted in the right conjunctival sac. The apex impulse of the heart was diffuse and heaving and located in the anterior axillary line. A short thrill, systolic in time, was palpated over the base of the heart. The area of cardiac dullness extended 14 centimeters to the left of the midsternal line in the fifth interspace and six centimeters to the right in the fourth interspace. The heart tones were regular and accelerated. The first sound at the apex was almost completely obscured by a harsh prolonged systolic blow which radiated outward into the axilla. A short presystolic murmur was also heard in this area. At the base of the heart very loud and distinct to and fro murmurs were heard. The blood pressure was 124 systolic and 30 diastolic. The radial pulse was regular and had a slapping, quick quality. The lung fields were resonant everywhere; the bases were on a level and descended about equally; no râles were heard anywhere. The abdomen was flat and soft; the liver and spleen were not felt; and there was no bulging or shifting dullness in the flanks. The extremities showed no edema and the joints appeared normal.

Laboratory Examinations. Blood Wassermann negative (Kolmer technic);

Kahn test negative; non-protein nitrogen 27 mg. per 100 c.c.; icterus index 12.5. Red cells 3,500,000, white blood cells 11,100, with 80 per cent polymorphonuclear cells. Hemoglobin 9.9 grams per 100 c.c. In the blood culture, many colonies of gram positive cocci appeared on the second day. These were later defined as streptococci of the viridans group. The urine was dark reddish brown; specific gravity 1.020; it contained a moderate amount of albumin, and there were red blood cells in moderate number in the centrifuged specimen.

Course. The temperature ranged from normal to 102° daily. The pulse was usually regular but extrasystoles were sometimes noted, and on several occasions coupled beats were felt. No digitalis was prescribed and none had been taken prior to admission. The pulse rate usually varied between 85 and 120 per minute; on one instance the rate was charted at 56 per minute. The patient appeared to gain strength, and aside from the extreme sweating and persistent weakness and dyspnea, he was fairly comfortable. On the eighth day following admission a transfusion was given at 10 o'clock in the morning with 500 cubic centimeters of citrated blood taken from patient's brother as donor. During the afternoon of that day the patient felt unusually well and commented on his improvement. He called attention to the fact that since the transfusion his bed no longer oscillated with each heart beat, which added to his comfort and peace of mind. At five o'clock in the afternoon the coupled beats were again noted at the radial pulse, and there had been a steady decline in the pulse rate from 112 at 8:00 a.m. to 76 at 6:00 p.m. At seven o'clock the patient's bed was rolled out on to the porch as usual and the patient was left smoking a cigarette. When the nurse returned five minutes later, she smelled the bedclothes burning, and noted that the cigarette had fallen from the patient's fingers to the bed. The patient was pulseless and respirations had ceased. A convalescing patient nearby had heard nothing to attract his attention. When questioned, he had heard no cough or cry and was entirely unaware that anything unusual had happened.

Comment. In attempting to explain the mechanism of such instantaneous death in a patient who had bacterial endocarditis, several possibilities were considered: coronary embolism, medullary embolism, pulmonary embolism, and rupture of the heart. The most likely explanation, however, was thought to be the interruption of the conduction impulses by the same infectious process which involved the endocardium, resulting in sudden complete heart block with ventricular standstill or fibrillation and death. As will appear, this was found to be the case.

Postmortem. (Dr. A. O. Severance.) At autopsy careful search of the blood vessels of the heart, brain, and lungs failed to reveal any emboli or thrombi. The findings of chief interest were in the heart, which weighed 640 grams. There were extensive warty vegetations on both the mitral and aortic valves as is shown in the photographs. Figure 1 shows the extremely large vegetations on the aortic leaflets and on the posterior surface of the mitral leaflets. The largest group of vegetations in the center of the photograph measured six by three centimeters and involved chiefly the posterior aortic leaflet and the under surface of the posterior mitral leaflets. Note also the rather shallow mycotic ulcerations which involved the endocardium just beneath the posterior aortic leaflet; the areas of greatest involvement and ulceration corresponded identically with the course of the bundle of His and the left branch of the auriculo-ventricular bundle.[9] Figure 2 shows the right auricle and the medial cusp of the tricuspid valve. Note a small area (a) just in front of the anterior attachment of the leaflet. This represents an ulceration nine millimeters in diameter which had extended entirely through the septum from the larger ulcerated areas beneath the aortic leaflets on the other side. Compare the location of this mycotic ul-

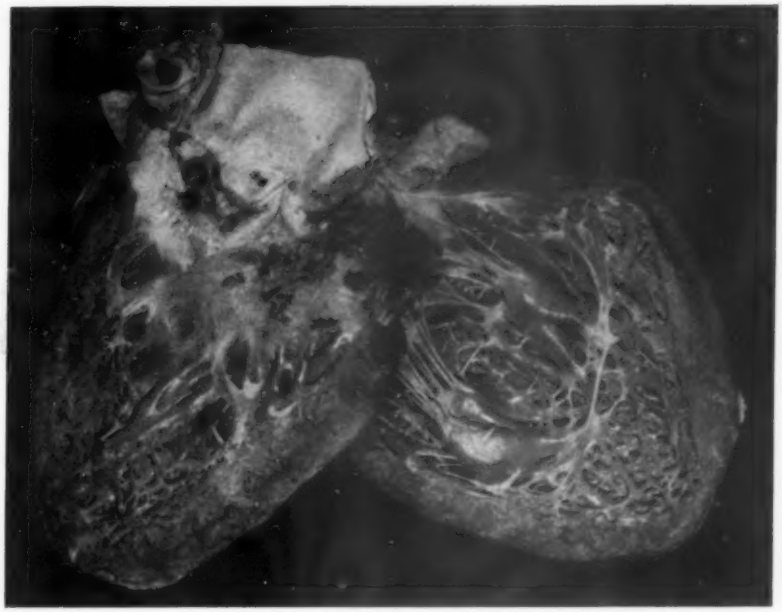

FIG. 1. The large vegetations on the aortic leaflets and posterior mitral leaflet are obvious. Note also the sub-endocardial ulcerations beneath the posterior aortic leaflet. These ulcerated areas overlie the course of the left branch of the bundle of His.

ceration with that of the auriculo-ventricular node as illustrated in figure 3, noting the relative positions in the two photographs of the ulceration and Tawara's node, the coronary sinuses, the fossae ovale, and the medial tricuspid leaflets. The corresponding positions of the ulceration and Tawara's node are striking.

REVIEW OF THE LITERATURE

Inflammatory lesions and degenerative processes interfering with the conduction of impulses through the junctional tissues have been cited in numbers. Rosenthal [2] has recently called attention again to the occurrence of acute isolated myocarditis in which the suppurative process may involve the conducting mechanism. He cited two instances which showed clinical signs of heart block and in each the inflammatory reaction involved especially the bundle of His. Both of his cases presented evidence of valvular endocarditis. Thayer [1] commented on the special frequency of mural endocarditis in subacute streptococcal endocarditis, and noted that aneurysms of the valves and perforations as a result of ulceration were relatively common. In a large series, however, he observed no instances where the specialized conducting tissue was involved. Rothschild et al.[3] observed that inflammatory lesions (Bracht-Waechter bodies) in the myocardium in subacute bacterial endocarditis are frequently inconspicuous and in general are without effect on intraventricular conduction. In a large number of electrocardiograms in patients with endocarditis they observed significant changes in the ventricular (QRST) complex in only one instance. Prolongation of the P-R interval was noted, however, in 10 of the 123 cases. On the

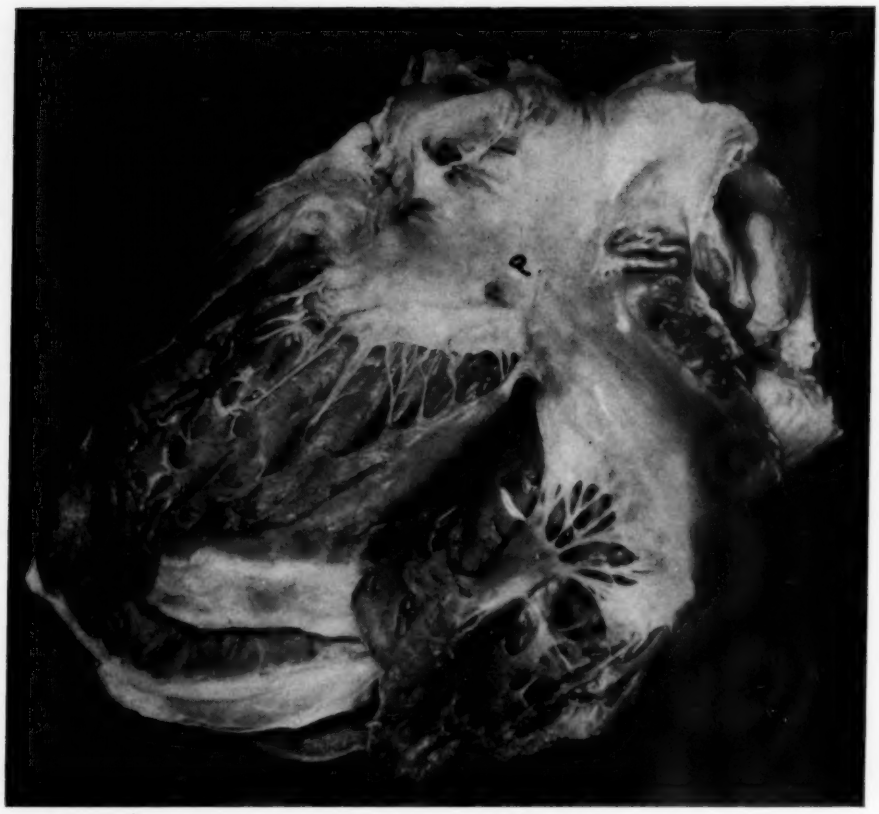

FIG. 2. This photograph shows the right auricle and ventricle and the medial cusp of the tricuspid valve. Note an area (*a*) just above the anterior attachment of the leaflet. This represents an ulceration about 9 mm. in diameter which had extended entirely through the septum from the larger ulcerated areas beneath the aortic leaflets.

other hand White [4] recognizes that bacterial endocarditis may, rarely, be accompanied by severe myocardial ulcerations. He writes: "In very rare cases the process may cause an aneurysm in, or a perforation through, the ventricular septum, or from the left ventricle into the right auricle, or even a rupture of the auricular wall, and, also rarely, invasion of the upper ventricular septal region may damage the auriculo-ventricular bundle (of His) to cause heart block." Blumer [5] noted the frequency with which the mural endocardium is involved in the pathological process in subacute bacterial endocarditis, but emphasized the relatively slight involvement of the myocardium in this disease. In the 150 autopsies he reported, only seven had microscopic evidence of acute infection of the myocardium and in none of these is any special note made of damage to the conduction system.

Mycotic aneurysms of the valves and shallow sub-endocardial ulcerations, then, occur quite commonly in subacute bacterial endocarditis but the myocardium is rarely perceptibly damaged in this disease. We have been able to find record of but four cases of bacterial endocarditis in the literature in which gross

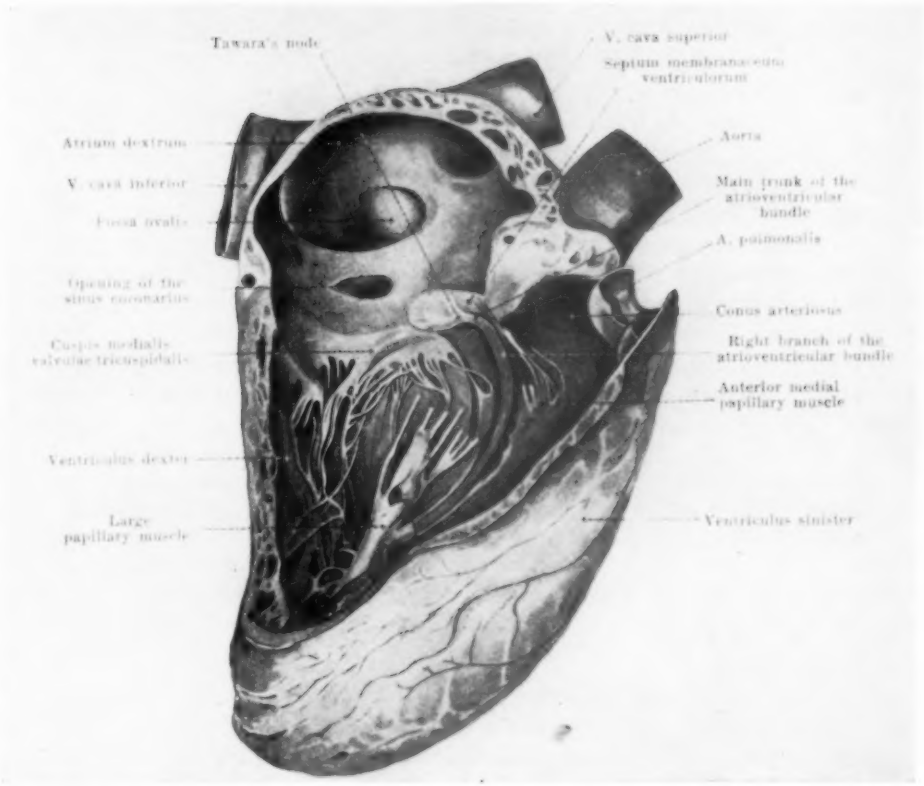

FIG. 3. This illustration (reproduced from Spalteholz) shows the location of the a-v node. Compare this illustration with figure 2, noting the relative positions in the two photographs of Tawara's node and the perforating ulceration, the coronary sinuses, the fossae ovale, and the tricuspid leaflets.

mycotic ulceration or aneurysm had interfered with the conducting mechanism.*

Wilson [6] reported three instances of vegetative endocarditis in each of which a mycotic aneurysm involved the interventricular septum. In two of these cases heart block had been diagnosed clinically and the region occupied by the bundle of His was found destroyed by the ulcerating process. Both of these patients died suddenly. Rothschild et al.[3] reported sudden death in a patient with bacterial endocarditis who had shown electrocardiographic evidence of partial bundle branch block. Necropsy revealed an aneurysm of the sinus of Valsalva caused by the spread of the bacterial infection from the aortic leaflets to the aorta. This aneurysm had projected into the interventricular septum and had partially

* Since this was written Dr. Warren Cooksey has called attention to a similar instance in his experience. A middle aged man had an atypical disease suggesting old rheumatic heart disease with a superimposed bacterial endocarditis. Electrocardiograms showed at first a markedly prolonged P–R time. Later the patient developed complete heart block (demonstrated graphically) and died after about three or four days. Autopsy revealed changes characteristic of old rheumatic heart disease and also fresh warty vegetations on the mitral leaflets. Just beneath the posterior aortic leaflet the vegetations had ulcerated through the septum into the right auricle completely destroying Tawara's node. This case was discussed at a State Clinical-Pathological Conference but has not been published.

intercepted the path of the left branch of the bundle of His. Stenstrom [7] reported a case of bacterial endocarditis in which there was definite clinical and electrocardiographic evidence of heart block on the patient's admission to the hospital. The first tracing showed complete auricular ventricular dissociation with an auricular rate of 73 and a ventricular rate of about 45; the P-R time was 0.45 second. Subsequent tracings showed the block to have disappeared and the P-R time decreased to 0.26 second. The patient had repeated anginal seizures and died suddenly some two months after admission. Sudden death in an anginal seizure was attributed to the necropsy finding of a thrombus in the anterior descending branch of the left coronary artery. Interestingly enough, a healing inflammatory lesion, of the same nature as the fresh endocarditis, was found localized in the tissue of the auriculo-ventricular node and the bundle of His. A correlation was noted between the stage of healing of this lesion and the previous functional recovery of conductivity as shown in the electrocardiograms.

Summary

Instant death in a patient with subacute streptococcal endocarditis is described. At autopsy a large mycotic ulceration was found to have eroded through from the left ventricle into the right auricle, largely destroying the region occupied by Tawara's node. Other sub-endocardial ulcerations intercepted the path of the left branch of the bundle of His. Instant death in this patient was thought to be due to the sudden onset of heart block followed by ventricular asystole or fibrillation.

REFERENCES

1. Thayer, W. S.: Studies on bacterial (infective) endocarditis, Johns Hopkins Hosp. Rep., 1926, xxii, 1–184.
2. Rosenthal, S. R.: Branch arborization and complete heart block, Arch. Int. Med., 1932, 1, 730–758.
3. Rothschild, M. A., Sacks, B., and Libman, E.: Disturbances of cardiac mechanism in subacute bacterial endocarditis and rheumatic fever, Am. Heart Jr., 1927, ii, 356–374.
4. White, P. D.: Heart disease, 1931, Macmillan, New York, p. 350.
5. Blumer, G.: Subacute bacterial endocarditis, Medicine, 1923, ii, 105–170.
6. Wilson, C. P.: Mycotic aneurysm involving intraventricular septum, Am. Heart Jr., 1926, i, 703–706.
7. Stenstrom, N.: Recovery from complete a-v block in case of endocarditis with post-mortem examination, Acta med. Scandinav., 1927, lxvii, 185–188.
8. Spalteholz, W.: Hand-atlas of human anatomy, 1923, J. B. Lippincott, Philadelphia, 5th ed., ii, p. 389a.
9. Lewis, T.: Mechanism and graphic registration of the heart beat, 1920, Paul B. Hoeber, New York, pp. 4–5.

SPLENIC VEIN THROMBOSIS AND ITS RELATIONSHIP TO BANTI'S SYNDROME; WITH REPORT OF A CASE *

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THE relationship between splenic vein thrombosis and Banti's disease has been much discussed and, like most unsettled questions, it is possible that the cause of disagreement lies in the different conceptions of what actually constitutes Banti's disease. On the one hand, many prefer to speak of the Banti syndrome and thereby testify to their belief that it is a group of symptoms and pathologic changes which may have several pathogenic factors. Among these factors they would include splenic vein thrombosis as primary. Others largely agree with Banti in his conception of a disease which progresses through the stages as described by him and is marked by pathologic changes which include splenic thrombophlebitis, not however as a primary factor. For several years many writers have suggested that the latter may occur independently of Banti's disease and that it may give rise to symptoms which indicate the diagnosis. A review of literature, however, leaves one with the impression that splenic vein thrombosis is an important part of the disease originally described by Banti. The following report illustrates the difficulty of diagnosis in those cases in which hematemesis is the outstanding feature.

CASE REPORT

The patient was a white woman, 28 years old, who was admitted to the hospital on September 23, 1933, complaining of severe epigastric pain, vomiting of blood and a bloody diarrhea. On the day preceding her admission, she had been in comparatively good health and had gone to work as usual; a few hours later she experienced a severe pain in the stomach, vomited a great deal of bright red blood and passed some fresh blood in her stool. She was taken to a local hospital where a diagnosis of bleeding gastric ulcer was made. An operation was advised but was refused. She placed herself under the care of a local physician who treated her for bleeding ulcer, using sedatives and ice bags. Under this treatment her symptoms subsided. The next morning on attempting to rise, she was again seized with severe abdominal pains, vomited blood and was then admitted to the Flower Hospital.

Her illness seems to have started in 1921, approximately 12 years before. At that time, she began to have fainting spells, at least one a day; she would become unconscious and while in this state, blood gushed freely from her mouth. Invariably this bleeding stopped before she regained consciousness. After these attacks, the patient complained of severe substernal burning, so much so that for a time she was treated for "heart burn," but without relief.

On February 27, 1924 while visiting a midwestern town, she complained of a pain in the stomach and fainted; while in this state she was rushed to a hospital and operated on. The surgical report was as follows: "The uterus, tubes and ovaries were normal in size and position. The appendix was turned on itself and bent in midposition and had several adhesions. It was five inches long, congested and thickened. Pathological diagnosis: chronic appendicitis."

The patient had rather a stormy recovery, remaining in the hospital for six weeks. During this time she complained of substernal burning, epigastric pain and the vomiting of blood. Seven months later, on her return to New York the patient

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From the Department of Medicine at Flower Hospital, Dr. P. J. R. Schmahl's Service.

was operated on for bleeding ulcers. Following this operation all of her symptoms were so aggravated that four months later another operation was performed; and again the patient found no relief. Unfortunately a report of the last two operative procedures was not obtained.

Her hematemesis, epigastric pain, fainting spells and general weakness became steadily worse and on September 8, 1925 she reëntered the same midwestern hospital for further treatment. On the day of her admission she was transfused and four days later another operation for recurrent gastric ulcers was done. This operation was reported to me as follows: "An old median scar was excised. There were dense adhesions of the omentum to the abdominal wall. All adhesions were separated and the stomach examined. The duodenal-pyloric junction was thickened. The ulcer scar was found at the greater curvature just above the entrance of the circulation. This ulcer was excised and the wound closed with double linen sutures. A short loop posterior gastro-enterostomy was done."

Again instead of getting better, the patient's condition became definitely worse. She was now unable to retain anything, vomiting blood and food almost continually. On December 5 another laparotomy was performed, of which the following summary report was obtained: "A midline incision was made and the old postoperative adhesions were broken down. The stomach was brought into the operative field and the old gastro-enterostomy scar excised. The stump of the intestines was sutured. Incision of the stomach sutured, the jejunum was replaced in normal position. Stomach opened and bleeding ulcer excised." Laboratory diagnosis: "Minute ulcers upon the duodenal mucosal surface, partially healed." This last operative procedure again failed to give the desired therapeutic results. It is interesting to note that during the last three operative procedures, the patient was pregnant and finally delivered a full term living child. Her symptoms continued with some modifications until the time of her present admission.

The past history of the patient brought out some very interesting points. She had had most of the childhood diseases, namely, diphtheria, chicken pox, scarlet fever, whooping cough and broncho-pneumonia.

On further questioning, the beginning of her illness was featured by the vomiting of bright red blood, burning sensation and occasionally a bloody diarrhea. Later a pain developed as an important symptom. This pain was first located in the epigastrium, was very sharp, had no relation to food, and was associated with a large tender lump in the left hypochondrium. After the vomiting of blood, the pain and the mass would tend to disappear, leaving only a sensation of soreness. The patient complained of profuse menstrual flows and dates all her trouble from the time her menses became profuse. Her fainting spells in the beginning of her illness were associated with hematemesis. About two years before her admission, there was a period of repeated chills, fevers and sweats, during which time she was treated for malaria without any relief. There had been a moderate loss of weight. She also complained of bruising very easily, so that at all times she showed subcutaneous hematomas. The family history was not remarkable.

On physical examination she was moderately well nourished, and revealed little of interest other than the findings in the abdomen. The abdomen showed the scars of the previous operations and was very sensitive throughout, both to light and deep pressure. There was some rigidity of the epigastric region; the lower margin of the spleen was palpable just below the costal margin. The liver was not palpable or enlarged. The pelvic examination revealed a chronic vaginitis and endocervicitis. The lower extremities showed numerous ecchymotic areas.

For a month following admission to the hospital the temperature, pulse and respirations were normal. Then chills, fevers and sweats developed and lasted for five weeks. The fever at times reached 104.5° F. with daily remissions.

Laboratory Studies. The vomited blood was bright red in color and faintly acid in reaction, suggesting that it might be coming from the esophagus or the upper part of the stomach.

Blood examination: The red blood cells numbered 3,750,000; the hemoglobin was 81 per cent and the color index 0.8. The white blood cells numbered 9,800, with polymorphonuclear neutrophiles 60 per cent; eosinophiles 4 per cent; lymphocytes 33 per cent and mononuclears 3 per cent. The platelet count was 220,000 on admission, and 115,000 the day after. The coagulation time was 5 minutes; the bleeding time 3.5 minutes, and clot retraction was marked within 3 hours.

There can be no doubt of the importance of the platelet count in this condition. In this case the count was made almost daily and in a general way it was noted that epigastric pain and hematemesis were more apt to occur when the platelet count had fallen to lower levels (table 1).

TABLE I

Relation of Platelet Count to Clinical Symptoms

DATE	PLATELET COUNT	SYMPTOMS
9-23-33	220,000	severe pain
9-25	115,000	severe pain
9-26	125,000	comfortable
9-28	135,000	comfortable
9-29	120,000	severe pain, hematemesis
9-30	135,000	severe pain, hematemesis
10-2-33	185,000	comfortable
10-9	205,000	comfortable
10-11	225,000	comfortable
10-18	190,000	severe hemorrhage
10-20	130,000	pain
10-23	115,000	pain
10-25	160,000	pain
10-31	140,000	pain
11-3	135,000	pain
11-6	170,000	pain
11-10	160,000	pain
11-13	225,000	pain, bleeding
11-17	200,000	comfortable
11-20	200,000	comfortable
11-22	operation	
11-27	265,000	no complaints
12-11	445,000	no complaints
1-13-34	300,000	no complaints

During the febrile period repeated blood cultures yielded no growth. Blood smears examined for both malarial and filarial parasites were negative. The Widal and Felix-Weil reactions were also negative.

The blood Wassermann reaction was one plus, but the Kahn reaction was negative. Blood chemistry: creatinine, 1.5 mg.; urea, 20.0 mg.; blood sugar, 109 mg.; uric acid, 4.0 mg.; calcium, 10.6 mg.

The urine showed numerous pus cells associated with *Trichomona vaginalis.* Roentgen-ray studies of the chest showed normal heart and lung shadows with a clear retro-cardiac space. The gastrointestinal series did not show any filling defects which might suggest an ulcer; though there was some barium retention in the stomach five hours after the beginning of the series. On November 20, 1933 esophagoscopy revealed two well formed varices present in the cardiac end of the esophagus.

In the foregoing the following might be emphasized: (1) The length of duration of symptoms, and their persistence following numerous surgical attacks on supposed peptic ulcer; (2) The pain in the epigastrium which was relieved by the vomiting of bright red blood; (3) The enlarged spleen, which grew larger just before an attack of pain and then decreased in size after the vomiting of blood; (4) The tendency to bruise easily, associated with a rather low platelet count; (5) The occurrence of chills, fevers and sweats; (6) The presence of esophageal varices.

In attempting to make a diagnosis in this case the possibility of peptic ulcer seemed unlikely because of the lack of roentgen-ray evidence, the persistence of symptoms after operation, and the atypical pain which had no relation to food but was relieved by the vomiting of faintly acid blood. Purpura hemorrhagica was eliminated by the normal bleeding, coagulation and clot retraction time, in spite of the presence of a relatively low platelet count and a palpable spleen. The severe substernal burning made us consider heart disease, but not seriously after the negative physical examination and the negative roentgen-ray findings in the chest. The chills, fevers and sweats occurring with regularity, and the presence of an enlarged spleen suggested chronic malaria, but repeated blood smears were negative.

Consideration of the history and examination suggested that possibly some interference with the return circulation of the spleen might account for the whole disorder. Such an obstruction would cause an increase in the collateral circulation through the short gastric veins leading to the formation of esophageal varices, and whenever the burden on the splenic circulation increased, the spleen would enlarge, causing an increased pressure in the varices which clinically might manifest itself as pain. Rupture of the varices would relieve this pain, and the patient would feel better. After healing of the ruptured varix, and restoration of blood volume the process would start over again. The causes of such an obstruction include thrombosis of the splenic vein due to unknown causes, a tumor pressing on the splenic vein, postoperative adhesions, a diffuse generalized fibrosis of the reticular system of the spleen, or a thrombophlebitis of the splenic vein. Because of the associated chills and fevers in this case, the latter was thought to be the cause, though it was considered possible that postoperative adhesions played a very important part. Thrombophlebitis having been agreed on as the most likely possibility, splenectomy was performed on November 22, 1933, and was followed by an uneventful recovery. The patient had no unusual abdominal pain following the operation.

Three months after the operation the patient was completely free of gastric symptoms. The vomiting of blood, the pain and substernal burning had stopped. Her general health was excellent. Immediately after the operation the platelet count rose to 445,000, the coagulation time four and one-half minutes, and the clot retraction was marked within seven hours. A blood count taken about two months after splenectomy showed: red blood cells 3,770,000, hgb. 77 per cent and color index 1.0. White blood cells 10,900, with polymorphonuclear neutrophiles 51 per cent, eosinophiles 2 per cent, lymphocytes 44 per cent, and mononuclears 3 per cent. The platelets numbered 300,000.

Dr. Earl Eaton, who performed the operation, remarked that he found multiple adhesions of the stomach and greater omentum to the anterior abdominal wall and liver in the upper right quadrant. The gall-bladder, duodenum and pylorus were covered by adhesions. The fundus uteri was adherent to the sigmoid by dense bands. The liver appeared normal; the gall-bladder thin-walled, emptied readily, and contained no stones. The stomach showed several scarred areas on its lesser curvature and anterior wall. The spleen was three times its normal size and showed areas of fibrosis throughout. The veins toward the stomach were large and varicosed.

The pathologic examination of the excised spleen was carried out by Dr. W. E. Youland who made the following report: The spleen measures 10 by 7 by 2 cm. It is fairly firm. On section considerable blood exudes. The venous channels are somewhat dilated. The Malpighian corpuscles stand out prominently, and the intervening tissue is dark reddish in color. Microscopic sections show dense cellular elements in the splenic interstices. A part of this cellular picture undoubtedly includes a marked hypertrophy of the endothelium of the sinusoids. It is impossible to identify with accuracy the type of cells present, except for a preponderance of eosinophiles which are scattered uniformly throughout the entire section. The sinuses are widely dilated. There is a considerable numerical increase in the lym-

phoid follicles. Virtually all of the follicles present appear to be inactive. In some of the follicles there is a definite, and in some, a marked increase in the number of lymphoblasts. In many follicles a homogeneous eosinophilic substance is present in the form of irregular anastomosing strands, resembling somewhat early formed amyloidosis. The central arterioles of the follicles as well as arterioles throughout the splenic tissue appear to be definitely thickened with a narrowing of the lumen. There are other areas showing a thinning out of the cellular element with apparently an increase of reticular fibrosis. The interstitial tissue throughout the sections as a whole suggests slight thickening, some sections showing more definitely fibrotic changes than others. The lymphoid follicles in other sections show a marked increase of red blood cells which may be considered as due to capillary congestion or possibly to erythrocytic infiltration. Oil immersion examination shows no definite phagocytosis of red blood cells. There are no megalokaryocytes present. The large blood vessels, especially the vein suggests a possible fibrous replacement of the wall and also some dilation. No other definite changes can be made out.

Discussion

As to the etiology of splenic vein thrombophlebitis very little can be said. It occurs in children.[6] Trauma may play an important part. Abdominal tumors which obstruct the flow in blood vessels, or local areas of degeneration and inflammation may be causative agents. Postoperative adhesions may also contribute. It has been suggested that physico-chemical factors in the splenic vein might in a way be responsible. Alteration in the platelet count can precipitate the so-called platelet crisis and lead to thrombus formation, as suggested by Rosenthal.[7]

There can hardly be doubt that a thrombus in the splenic vein can produce the clinical picture which has been described as characteristic of thrombophlebitis of the splenic vein. The report by Frick,[8] with the associated autopsy findings is important in this connection. On the other hand Warthin[16] and McMichael[3] have been unable experimentally to produce this picture in laboratory animals; and Wohlwill[9] showed that the presence of a definite thrombus in the splenic circulation did not necessarily produce an enlarged spleen.

The original writings of Banti,[1] quoted by Warthin,[16] suggested that splenic or portal vein thrombosis was a constant factor in Banti's disease and it is because of this factor that these two conditions were thought to be the same.

On the other hand Vertan,[10] McMichael,[3] Evans,[11] and Bryce[12] though describing a clear cut clinical picture of Banti's disease, have been unable to find definite evidences of thrombosis in the splenic circulation and therefore have suggested that thrombophlebitis of the splenic vein is entirely different from Banti's disease. The failure of these investigators to find the splenic vein lesion might be explained by the fact that practically all of their work has been done on spleens which were removed at operation and most of these workers did not thoroughly investigate the splenic and hepatic circulations. Moschcowitz[13] attempted to show that Banti's disease was in reality a complex syndrome wherein any one stage of the disease might dominate the clinical picture. Microscopic studies in splenic vein thrombophlebitis have shown a marked resemblance to the splenic picture of real Banti's. There is a moderate proliferation of the reticulo-endothelial system with some dilation of the sinuses. The Malpighian corpuscles show some fibrosis of the central artery, and some hyaline changes, and though endophlebitis is rare, it is occasionally seen. The blood vessels show

some fibrosis, and a narrowing of the lumen. An occasional siderotic nodule is present indicating hemorrhage.

The symptomatology of splenic vein thrombophlebitis is characterized by chronicity, gastric distress and hemorrhages, an enlarged spleen, and symptomatic relief after the vomiting of blood. A mild anemia and the demonstration of esophageal varices help to make the diagnosis certain. Because of the multiplicity of symptoms which these patients present, a careful differential diagnosis must include a consideration of peptic ulcer, hemorrhagic diseases, heart disease, chronic malaria, parasitic diseases of the spleen, and advanced Banti's disease.

The prognosis is poor in untreated cases, as the patient will eventually die from a severe hemorrhage. Following splenectomy recovery and comparatively good health usually result.[14] The preoperative platelet count is important.[12] It has been shown [7] that where the count is high the mortality of splenectomy is markedly increased, the patients usually dying of a massive portal thrombosis, probably related to the tremendous rise in the platelet count following operation. Preoperative transfusion is of course indicated in very anemic patients.

Conclusions

1. Splenic vein thrombosis is essentially a phase of Banti's disease.
2. It is characterized by chronicity, an enlarged spleen, vomiting of blood which gives symptomatic relief, a moderate anemia and esophageal varices. The splenic tumor decreases in size after a hemorrhage.
3. It is amenable to surgical removal of the spleen.
4. The surgical risk is in direct proportion to the platelet count; the higher the count, the poorer the prognosis.

REFERENCES

1. Banti, G.: Quoted by Warthin.[16]
2. Gray, H.: Anatomy of the human body, 1930, Lea and Febiger, Philadelphia.
3. McMichael, J.: Local vascular changes in splenic anemia, Edinburgh Med. Jr., 1931, xxxviii, 1–29.
4. Hertheimer, G.: Berlin. klin. Wchnschr., 1917, 82.
5. Boyd, W.: Surgical pathology, 1933, W. B. Saunders Co., Philadelphia.
6. Smith, R. M., and Howard, P. J.: Early occurrence of gastric hemorrhage in children with splenomegaly, Am. Jr. Dis. Child., 1927, xxxiv, 585–594.
7. Rosenthal, N.: Clinical and hematologic studies on Banti's disease, Jr. Am. Med. Assoc., 1925, lxxxiv, 1887–1891.
8. Frick, A.: Chronic splenomegaly, Jr. Am. Med. Assoc., 1922, lxxviii, 424–425.
9. Wohlwill, F.: Über Pfortadersklerose und Bantiähnliche Erkrankungen, Virchow's Arch. f. path. Anat., 1925, ccliv, 243–271.
10. Vertan, E.: Bericht über einen durch Milz Venenthrombose bedingten Fall von Splenomegalie, Zentralbl. f. Chir., 1930, lvii, 1342–1344.
11. Evans, W. H.: Blood platelets in splenic anemia, with special reference to treatment by splenectomy, Lancet, 1929, i, 277–282.
12. Bryce, A. G.: Lancet, 1932, xi, 1423–1425.
13. Moschcowitz, E.: Banti's disease, Jr. Am. Med. Assoc., 1917, lxix, 1045.
14. Osler, W. H.: Modern medicine, Vol. 3, 1925, Lea and Febiger, Philadelphia.
15. Rolleston, H. D.: Chronic splenic anemia and Banti's disease, Practitioner, 1914, xcii, 470.
16. Warthin, A. S.: Relation of thrombophlebitis of the portal and splenic veins to splenic anemia and Banti's disease, International Clin., 1910, iv, 189–226.

ALLERGIC CORYZA AT MENSTRUATION FROM OVARIAN HORMONE*

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THE symptoms which may be associated with menstruation are numerous and varied. The majority of them are plainly the result of the cyclic functional and structural changes in the genital tract; but occasionally the history suggests an allergic basis for the phenomena. Such a case is described here.

CASE REPORT

E. S., married, a white female aged 29, complained of frequent attacks of coryza; these began regularly the day before or the first day of her menstrual period. The initial symptoms were malaise and frontal headache, and these were followed by sneezing, nasal obstruction, chills, fever of about 101°, and prostration. Within 24 hours of the onset the patient had been confined to her bed during every menstrual period for one year. The disability would continue for about two days, to be followed by symptoms diminishing in intensity for three or four more days. The thickness of the nasal discharge was varied, and occasionally was burning to the nostrils. There was no lachrymation. Ephedrine gave moderate relief.

For about the same length of time a tachycardia averaging 140 beats per minute had been present for brief periods. This was most marked during or following the coryzal attacks, but also occurred at other times. Diligent search had been made for an etiological agent here, but without results. Roentgen-rays of the teeth, sinuses and chest were all negative; the heart was normal in size, sounds and contour. The Kahn test was negative and the basal metabolic rate normal.

Menstrual History: The periods began at 13 years and were regular at once, being of the 28/5 day type. Two children have been borne. For the last four periods of the present illness the intervals had changed to a 24/2 day type.

Family and Past History: The maternal grandfather had had "miner's asthma." There were no other hereditary factors apparent. The patient herself has noticed a sensitivity to absorbent cotton for years, the latter producing symptoms of coryza.

In the belief that the coryza might be allergic, certain cutaneous and therapeutic tests were made as follows:

On November 10, 1933, which was seven days following the first day of the last menstrual period, a cutaneous scratch test was made using an aqueous solution of crystalline folliculin as a test reagent and with an alkaline solution for a control. A faintly positive reaction was elicited.

On November 13 and 16, the test was repeated and faintly positive reactions were again elicited. On November 19 and 22, tests were negative.

The patient was menstruating and was bedfast on November 27. On December 2, 7, 10 and 12, cutaneous tests were negative. December 3 to 6 of this period, the patient was suffering from acute rhinitis, apparently not related to the condition being discussed.

On December 14, one c.c. of aqueous solution of folliculin (theelin) was injected subcutaneously. Six hours later malaise and chills appeared, to be followed by a coryza similar to, but not quite so intense as that of the menstrual period. This remained until December 18. On December 20, the patient began to menstruate but had no evidences of coryza. One c.c. of folliculin was readministered; this was enough to elicit mild symptoms of coryza. The menstruation ceased on December 22. On December 25, folliculin was again injected and was promptly followed by a coryza which lasted for two days.

* Received for publication May 21, 1935.

On January 8, one c.c. of folliculin was sprayed on the nasal mucosa. This gave rise to a coryza within 30 minutes, which lasted through January 9.

On January 10, the patient being free from symptoms, folliculin was again administered intranasally. Symptoms reappeared promptly to last through January 11 and 12. On January 15, folliculin was administered subcutaneously; this brought forth a very slight reaction. From January 16, to 19, the patient was menstruating and was free from symptoms for the first time in over a year.

From January 25 to March 31 exclusive, 13 doses of folliculin were administered by means of vaginal suppositories at from three to five day intervals. On two of these occasions mild symptoms of malaise appeared; on the other days there was no reaction whatever.

From February 10 to 14 and again from March 14 to 18 normal menstruation took place.

Our evidence that the coryza is allergic may be summarized thus:

(1) A positive cutaneous reaction (though not marked) was secured.

(2) The allergic manifestation was artificially reproduced at will by the administration of folliculin.

(3) Tolerance to the agent was secured by repeated administrations which resulted in the total relief of symptoms.

It would seem, therefore, that in this case folliculin has been proved to be an allergic agent, giving rise to a coryza at the menstrual period, by some mechanism which we are not prepared to explain.

EDITORIALS

EMOTIONS AND BODILY CHANGES

THE appearance just recently of an extensive bibliography [1] upon the subject of the relation of the emotions to bodily changes should help to stimulate further thought among internists upon the status of this problem in the practice of medicine. The consultant internist especially will be interested since a large fraction of consultant practice is made up of those cases which present the problem of assessing the proportionate parts played by psychic and somatic factors in the development of the patient's disability. Both factors we have come to believe are involved in most cases but in some the dominant rôle is played by organic disease and in some by the psychic disturbance. The nature of these complex interrelationships is still all too obscure. A better understanding of their scope, a deeper insight into their modus operandi are urgently needed to bring this lagging wing in line with the front of medical advance.

In the field of diagnosis the question presents itself to the practising physician almost daily in this form:

> How may disturbances in bodily function not accompanied by known structural changes in the tissues, but associated with important disturbances in the psyche, be differentiated from disturbances in bodily function which are associated with important structural changes and are accompanied by relatively minor disturbances in the psyche?

The usual method of procedure is to obtain a careful record of the symptoms, from the patient's own account of them and by observation of the objective phenomena which are detectable during their occurrence; and, further, to determine if possible, by physical examination and by special tests the nature of the functional abnormalities and the presence or absence of structural changes. These methods are carried out with varying degrees of thoroughness and skill according to the ability of the physician, the intelligence of the patient, and the availability of the special tests involved.

The study of the psychical component of the illness is of course of equal importance in such a differentiation. Skill in this study is certainly rarer than is skill in the study of objective bodily phenomena. There is current among psychiatrists an impression that the average physician totally ignores the importance of such a study. This is certainly an unfortunate error dependent in part upon the isolation of the average psychiatrist from the field of general practice and in part upon the fact that he sees very much more of the failures of the practitioner than of his successes. In part too it may be due to the fact that methods of study vary so widely in this field and that the busy practitioner's "sizing up" of the patient's situation and of his

[1] DUNBAR, F. H.: Emotions and Bodily Changes. A Survey of Literature on Psychosomatic Interrelationships 1910–1933. Published for The Josiah Macy Jr. Foundation, Columbia University Press, New York, 1935.

psychic reactions to it, seems too crude to the psychiatrist to be given any credit at all. Yet to those who are in closer touch with the realities of medical practice it will not seem an exaggeration to state that those physicians who attain success in general practice are almost universally possessed of a keen discrimination in differentiating the psychic disturbances which are dominant in a disease picture of functional type from those which are merely associated with important organic disease. Nor will it seem exaggerated to say that lasting success in general practice is largely dependent upon efficient discrimination of this type.

The method described above as being that in general use for solving the question as to the differentiation of these cases in which psychic and somatic disturbances coexist is dependent for its efficiency upon the existence of detectable differentiae between functional somatic disturbances due to organic disease and those not due to organic disease; and likewise between psychic disturbances whose causes lie in the relations of the psyche to the external environment in the broadest sense, and those which have arisen in response to somatic dysfunctions.

It must be acknowledged that while the accuracy of diagnosis of non-organic functional disturbances is well supported as a rule by the observed later course of these patients, this is less uniformly true of our diagnosis of organic disease. We still urgently need new methods of differentiation. Too many gross errors are still made in both directions; too many cases treated with drugs or by surgical procedures for conditions requiring primarily psychiatric care; and too many organic conditions passing undetected under the guise of neuroses.

The question arises whether the advance will be made by further perfection of the methods of somatic diagnosis or by progress in the field of psychiatric study.

Many have stated that from the point of view of immediate improvement in the existing level of medical practice in this respect the most urgent requisite is that more psychiatric training should be given to medical students since the average physician is undoubtedly weaker on this side than in his knowledge of the structural aspect of disease. This is no doubt true and the present widespread tendency to increase the time devoted to psychiatry in the curriculum will be justified.

Ultimately, however, it is questionable whether psychiatry, at least in any of its present forms, will furnish the practitioner with a further advance in method of study of such problems beyond what is now available. At least one may say that Dunbar's compilation of the writings of psychiatric authors in the last twenty-three years on psychosomatic interrelationships contains very little which promises further help. It appears to be a surprisingly uncritical literature, devoted in large part to semi-philosophical speculations, inclined too often to deal with assumptions as if they were proved facts, and betraying in its fertility as to terminology an attempted compensation for its sterility as to tangible accomplishment. We have

learned more in these last twenty years of the nature of the relationship between mind and body from a few physiologists such as Pavlov and Cannon than from all the psychiatrists. It is not to be wondered at. Emotions per se are immeasurable and imponderable, but their repercussions upon bodily behavior lend themselves to quantitation. It seems probable that as the mechanisms which bring about these bodily changes become better known we shall find in them distinctive characteristics of a measurable nature which will differentiate them from those mechanisms set at play through the mechanical, toxic or metabolic effects of inflammatory, neoplastic, or degenerative diseases.

DINITROPHENOL AND CATARACT

In our next issue there will be published a brief report on eight cases of rapidly developing cataract appearing in relatively young women during or shortly after treatment with dinitrophenol for obesity. With the consent of Dr. W. W. Boardman, the author, this advance notice is given to our readers of this new danger associated with the use of this drug. Its employment in the Stanford Clinic has been discontinued.

REVIEWS

The Principles and Practice of Neurology. By ALEXANDER CANNON and E. D. TRANCHELL HAYES. xx + 333 pages, with 114 illustrations. William Heinemann, Ltd., London, England. 1934. Price 25 s.

In the preface the authors state that "the purpose of this book is to present to the student and practitioner of neurology the essentials in the clinical examination, diagnosis, and treatment of nervous diseases." On the first score they have succeeded admirably. The first 55 pages are devoted to the clinical examination. The authors chose wisely in having Professor G. H. Monrad-Krohn present this important section. It is a careful, concise presentation on the methods of examination and is actually an abridged presentation of this author's excellent textbook, "Clinical Examination of the Nervous System." Any student mastering these chapters should be able to do a careful and intelligent examination. The method presented is essentially the one used and taught by the British School of neurologists. Professor Monrad-Krohn, although a Norwegian, has studied extensively in England. This chapter includes a few pages on history taking, discussion of cranial nerves, motor system, sensory system, and reflexes. The appendix to these chapters includes the electrical examination and an excellent discourse on aphasia.

Part II of the text presents the major neurological disorders of the nervous system. The plan of these chapters is very disturbing and will undoubtedly be grossly confusing to students. Obviously it is a very difficult task to present the subject of neurology in a single volume, consequently some orderly and logical grouping of diseases is the first requirement. This seems to be entirely lacking. Chapters 2 and 3, for instance, cover thirteen entities, ranging from exophthalmic goiter to the neuralgias.

Chapter 4 discusses the hereditary and familial nervous diseases. This grouping has the advantage of impressing the student with the magnitude of this great group of diseases. On the other hand, it would seem difficult for the beginner because of the lack of anatomical and pathological grouping. Diseases such as the myopathies have little in common with Wilson's disease, for instance, except the common factor of being hereditary affections.

Under the heading of "Epidemic Diseases of the Central Nervous System" in Chapters 5 and 6, both epidemic and non-epidemic subjects are discussed. Further, it is difficult to see why cerebellar palsies in children and hydrocephalus should be classified in this section. Many other such odd groupings will be found throughout the book.

In the discussion of each disease, a uniform plan is adhered to: definition, etiology, signs and symptoms, differential diagnosis, prognosis and course, and treatment. Many of these disease pictures are clearly drawn, notably multiple sclerosis. Very little emphasis has been placed on treatment. The treatment of subacute combined degeneration seems very inadequate. In the treatment of Meniere's disease, no mention is made of surgical section of the eighth nerve.

The book as a whole does not seem to be an ideal student's text, and is not detailed enough for a reference work. J. G. A., JR.

Disease, Gadfly of the Mind. By WILLIAM ALLEN PUSEY, A.M., M.D., LL.D. 20 pages; 17.5 × 24.5 cm. H. K. Lewis and Co., Ltd., London. 1934.

"That which has led us to where we are is not the beckoning of a plump and genial angel . . . but shrewd prods from the sharp stick of necessity." The author's thesis, in this the Prosser-White Oration before the St. Johns Hospital Dermatological Society, is that diseases as a goad to thought have been among the most active

agents in the making of the mind and that among diseases few have been so powerful in this respect as diseases of the skin. The development historically of this thesis constitutes the body of this most interesting address. M. C. P.

The Care of the Aged, the Dying, and the Dead. By ALFRED WORCESTER, M.D., Sc.D. vi + 77 pages; 13 × 18 cm. Charles C. Thomas, Springfield, Illinois. 1935. Price, $1.00.

Lectures from which the student and the practitioner alike may derive a broader and finer conception of the physician's rôle in the care of those whom he cannot cure.

The Harvey Lectures, 1933–1934, Series XXIX. By R. E. DYER, W. MANSFIELD CLARK, ROSS G. HARRISON, E. A. DOISY, EVARTS A. GRAHAM, GEORGE L. STREETER, THOMAS M. RIVERS, and DETLEV W. BRONK. 262 pages; 14 × 20.5 cm. Williams and Wilkins Company, Baltimore. 1935. Price, $4.00.

The Harvey Lectures are seldom light summer reading for the tired practitioner. Indeed the alert internist will find many of them outside the scope of his interests if not of his comprehension. In the present volume, however, there are a number of papers of the greatest value to all students of medicine. The lecture by R. E. Dyer on "Typhus and Rocky Mountain Spotted Fever in the United States" is an authoritative statement of the broad outlines of this important health problem. Most stimulating also are the lectures by Rivers on the filterable viruses, by Graham on "Clinical Application of Some Recent Knowledge of the Biliary Tract," and by Doisy on "The Estrogenic Substances." The lecture by Bronk on "The Nervous Mechanism of Cardiovascular Control" is a beautifully clear exposition of experimental investigations of circulatory regulating mechanisms which have only recently been discovered. This lecture in itself would make the volume a worthwhile addition to any internist's library. M. C. P.

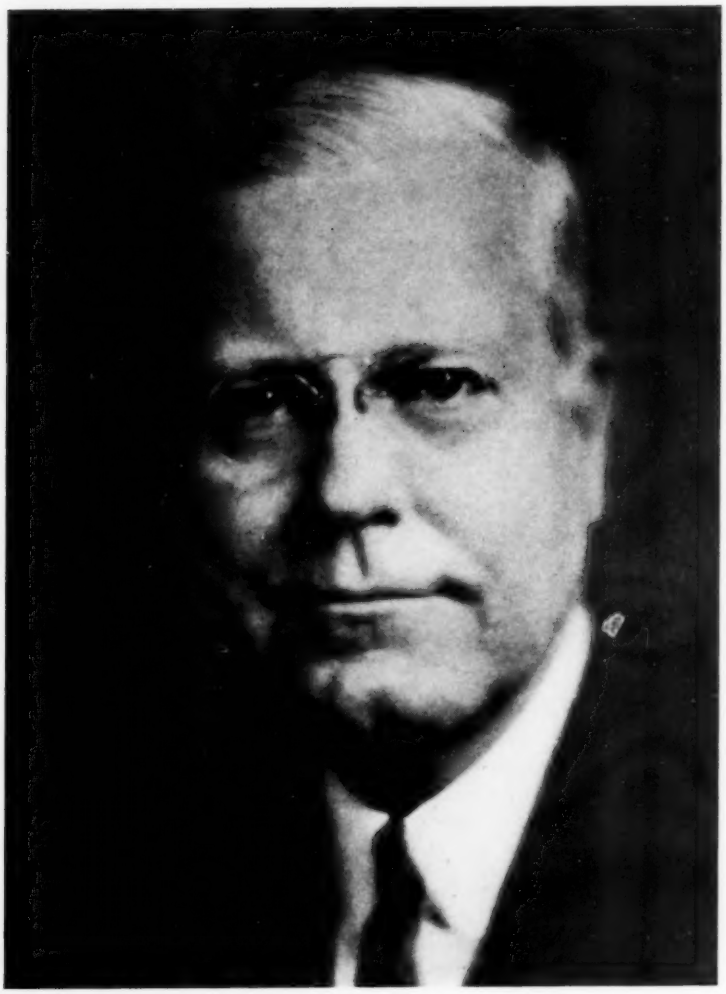
Treatment by Diet. By CLIFFORD J. BARBORKA, B.S., M.S., D.Sc., F.A.C.P. 615 pages; 15 × 23 cm. J. B. Lippincott Co., Philadelphia. 1934. Price, $5.00.

This is a well-organized book on diet. The chapter on The Application of Dietotherapy contains useful photographs illustrating comparative servings of typical foods. There is little discussion of the basic principles of nutrition or of the origins and uses of individual foodstuffs, the major portion of the work being a description of the diets useful in individual diseases. The book is filled with many sample diets. The author makes a useful distinction between diseases in which diet is of paramount importance and conditions in which it is of varying importance. An appendix contains the usual food tables and a few recipes. There is a good bibliography and adequate index. G. A. H.

Simplified Diabetic Management. By J. T. BEARDWOOD, JR., and HERBERT T. KELLY. 211 pages; 19.5 × 13 cm. Second Edition. J. B. Lippincott Co., Philadelphia. 1934.

The unusual feature of this diabetic manual is the "Unit Method" developed by the authors for calculating the diabetic diet, which seems to be an adaptation of the "Line-ration scheme" introduced by Lawrence and widely employed in Great Britain. It is used in conjunction with a somewhat elaborate "Diet Prescription Chart" which automatically gives the proper diet formula, according to the authors' conception, as well as the number of food 'units' required to prepare it.

The book contains the usual subject matter to be found in diabetic manuals of this type, and in general the material is presented clearly. It is interesting that the modern conception of shock in diabetic coma and the measures required for treating it, a matter which most students now believe is quite as important as the factor of acidosis, receive almost no consideration at all. Electrocardiograms are advised in all cases in which surgery is contemplated so that "cases of early coronary disease may be discovered." The book contains tables of food values and a list of recipes. G. A. H.



JAMES ALEXANDER MILLER, A.B., A.M., M.D., Sc.D., F.A.C.P.
NEW YORK CITY

PRESIDENT OF THE AMERICAN COLLEGE OF PHYSICIANS 1935–1936

JAMES ALEXANDER MILLER, A.B., A.M., M.D., Sc.D., F.A.C.P., NEW YORK CITY

PRESIDENT OF THE AMERICAN COLLEGE OF PHYSICIANS
1935–1936

Born, Roselle, N. J., March 27, 1874; graduated from Princeton University, A.B., 1893; A.M., same, 1894; College of Physicians and Surgeons of Columbia University, M.D., 1899; Columbia University, Sc.D., 1930.

Dr. Miller interned in the Presbyterian Hospital, New York City, 1899–1901. He has been connected with Bellevue Hospital since 1903. He began as Assistant Visiting Physician in General Medicine, First Division, later being promoted to Visiting Physician, holding this appointment for ten years; whereupon he became Visiting Physician in charge of the Tuberculosis Service, resigning his former position in General Medicine. This latter position he has held continuously for more than twenty years.

For the past fifteen years, Dr. Miller has been Professor of Clinical Medicine in Columbia University College of Physicians and Surgeons. He is Consultant to the New York Postgraduate Medical School and Hospital, to the Methodist Episcopal Hospital, to the Trudeau Sanatorium and to Sprain Ridge. He is also Consultant in Tuberculosis to the Presbyterian Hospital.

Dr. Miller has been President of the New York Tuberculosis Association, the National Tuberculosis Association and the American Clinical and Climatological Association. He is a Trustee of the New York Academy of Medicine, and has been Chairman of its Public Health Committee for the past fifteen years. He is President of the Board of Trustees of the Trudeau Sanatorium. During the World War, he was Medical Director of the Rockefeller Tuberculosis Commission in France, and was Major of the American Red Cross. He received the decoration of Chevalier Legion d'Honneur. He is a member of the Central Council Charity Organization Society, a member of the Board of Managers of the Association for Improving the Condition of the Poor and a member of the Technical Board of the Milbank Memorial Fund. In addition, Dr. Miller is a member of the New York Medical and Surgical Society, the New York Practitioners Society, the American Association of Thoracic Surgery, the American Clinical and Climatological Association, the New York Academy of Medicine, the American Medical Association and the Association of American Physicians. He is also a member of the University, Century and Deepdale Clubs.

Dr. Miller is the author of a large number of scientific articles dealing primarily with diseases of the chest, especially tuberculosis. He contributed the chapter on "Chronic Pulmonary Disease" in Musser's *Internal Medicine*, published by Lea and Febiger; he contributed the chapter on "Pulmonary Tuberculosis" in Nelson's *System of Medicine*.

Dr. Miller became a Fellow of the American College of Physicians in 1926, and has served on its Board of Regents since 1928. He has been particularly active on its Committee on Public Relations and its Committee on Finance. He enters upon his term as President with an intimate knowledge of the College's problems, and with a deep appreciation of the responsibilities of the organization.

ERNEST B. BRADLEY, A.B., M.D., F.A.C.P.
LEXINGTON, KY.

PRESIDENT-ELECT OF THE AMERICAN COLLEGE OF PHYSICIANS 1935–1936

ERNEST B. BRADLEY, A.B., M.D., F.A.C.P.
LEXINGTON, KY.

PRESIDENT-ELECT OF THE AMERICAN COLLEGE OF PHYSICIANS 1935–1936

Born, Lexington, Ky., May 16, 1877; educated in the Lexington Public Schools; Transylvania University, A.B., 1895; Postgraduate study in Chemistry, University of Kentucky, 1895–1896; Instructor in the Fayette County (Ky.) Schools and the Lexington City School System for five years; University of Michigan Medical School, M.D., 1904; Interne, New York City Hospital, 1904–1905; postgraduate research work in New York City, 1906. Dr. Bradley has practiced medicine in Lexington, Ky., since 1907. He has held the following appointments: City Bacteriologist, Lexington, 1908–1925; Part-time Health Officer, Fayette County (Ky.), 1909–1924; Chairman, Fayette County Board of Health, 1924 to date; Member, Lexington City Board of Health, 1932 to date; Visiting Physician, St. Joseph's Hospital and Good Samaritan Hospital, 1907 and 1909 to date, respectively; Member, Medical Advisory Board, Julius Marks Sanatorium (for Tuberculosis), Lexington, 1921 to date.

Dr. Bradley is a member and ex-President of the Fayette County Medical Society, an ex-President of the Kentucky Midland Medical Society, a member of Kappa Alpha and Nu Sigma Nu fraternities, member of the Kentucky State Medical Association, Fellow of the American Medical Association, member, ex-Vice Chairman, ex-Secretary and ex-Chairman of the Section on Medicine of the Southern Medical Association and member of the American Clinical and Climatological Association. During the World War, he was Major in the Medical Corps of the U. S. Army, acting as Chief of Medical Service of X-section, Camp Jackson, Columbia, S. C., and for a time was Chief of Medical Service at the Henry Ford Hospital, Detroit, Mich. He has been a member of the Lexington Clinic since its organization in 1920.

Dr. Bradley became a Fellow of the American College of Physicians in 1919. He served as the Governor for the State of Kentucky since 1926, and as Chairman of the Board of Governors since the death of the former Chairman, Dr. W. Blair Stewart, of Atlantic City, in 1933. For a number of years, Dr. Bradley has been a member of the Committee on Credentials, where he has given unstintingly of his ability and time.

COLLEGE NEWS NOTES

Gifts to the College Library

Acknowledgment is made of the receipt of the following donations to the College Library of publications by members:

Dr. Edward Schons (Fellow), St. Paul, Minn.—1 reprint;
Dr. Arthur A. Shawkey (Fellow), Charleston, W. Va.—1 reprint;
Major James S. Simmons (Fellow), Ancon, C. Z.—1 reprint.

Dr. J. K. Pepper (Fellow), Winston Salem, N. C., was elected first Vice-President, Dr. L. B. McBrayer (Fellow), Southern Pines, N. C., was reëlected Secretary-Treasurer, Dr. Wingate M. Johnson (Fellow), Winston Salem, N. C., was elected a member of the House of Delegates to the American Medical Association for two years, and Dr. C. C. Carpenter (Fellow), Professor of Pathology, Wake Forest College, was appointed Chairman of the Committee on Cancer for the ensuing year.

Dr. Allen H. Bunce (Fellow), Atlanta, Ga., has retired as Secretary-Treasurer of the Medical Association of Georgia after 15 years.

Dr. Paul H. Ringer (Fellow), Asheville, N. C., was inducted as President of the Medical Society of the State of North Carolina at their meeting in Pinehurst in May. Dr. P. P. McCain (Fellow), Sanatorium, N. C., was the retiring President.

Dr. Verne S. Caviness (Fellow), Raleigh, N. C., and Dr. J. Buren Sidbury (Fellow), Wilmington, N. C., were guest speakers at the spring meeting of the Third District Medical Society of North Carolina, held at Jacksonville, N. C., May 31.

Dr. Bernard L. Wyatt (Fellow), Tucson, Ariz., addressed the annual meeting of the Nebraska State Medical Association at Omaha, May 14 to 16, on "The Treatment of Chronic Arthritis" and "The Economic Aspects of Chronic Arthritis."

Dr. Frederick T. Lord (Fellow), since 1930 Clinical Professor of Medicine at Harvard University Medical School, has retired from the faculty as Professor Emeritus.

The Fifth Annual Fever Conference for physicians and others interested in the production of fever by physical methods and its use in the treatment of disease was held at Dayton, Ohio, May 2 to 3. Among those who addressed the meeting were: Dr. Philip S. Hench (Fellow), Rochester, Minn., "Results of Fever Therapy for Gonorrheal Arthritis, Chronic Infectious (Atrophic) Arthritis and Other Forms of 'Rheumatism'"; Dr. Walter M. Simpson (Fellow), Dayton, Ohio, "Report of Fever Therapy Research at Miami Valley Hospital"; Dr. Frank H. Krusen (Associate), Philadelphia, Pa., "Studies of Blood Picture Before and After Fever Therapy"; Dr. Ralph H. Kuhns (Associate), Chicago, "Present Status of Fever Therapy for Dementia Paralytica in the State Hospitals of Illinois."

Dr. William A. White (Fellow), Professor of Nervous and Mental Diseases at George Washington University School of Medicine, and Superintendent of St. Elizabeth's Hospital, Washington, D. C., delivered a series of three lectures known as the Thomas William Salmon Memorial Lectures at the New York Academy of Medicine during April.

Dr. David A. Tucker, Jr. (Fellow), Associate Clinical Professor of Contagious Diseases at the University of Cincinnati College of Medicine, has been appointed Professor of the History of Medicine in the same institution.

Dr. Philip F. Barbour (Fellow) and Dr. Thomas Cook Smith (Fellow) were among those on the teaching staff of the Children's Free Hospital, Louisville, Ky., where a 10 weeks' course in Pediatrics has been conducted under the auspices of the American Academy of Pediatrics. The course extended from April 24 to June 26.

Under the Presidency of Dr. Samuel E. Thompson (Fellow), Kerrville, Texas, the 69th Annual Meeting of the Texas State Medical Association was held in Dallas, May 14 to 16. Among guest speakers were the following: Dr. Joseph L. Miller (Fellow), Chicago, "Recent Advances in Our Knowledge of the Thyroid Gland"; Dr. Horton R. Casparis (Fellow), Nashville, Tenn., "Allergy in Children"; Dr. Arthur U. Desjardins (Fellow), Rochester, Minn., "Radiotherapy for Acute and Chronic Inflammatory Conditions"; and Dr. Albert C. Broders (Fellow), Rochester, Minn., "Cancer as We Comprehend It."

Dr. Charles W. Burr (Fellow), Professor Emeritus of Nervous and Mental Diseases, University of Pennsylvania School of Medicine, was the recipient of the twelfth annual Strittmatter Award of the Philadelphia County Medical Society recently. A bronze tablet bearing the names of three benefactors of the County Society was unveiled. The names included were Dr. Isidor P. Strittmatter, donor of the award, Dr. James M. Anders (Master), founder of the Library, and the late Dr. Lawrence Webster Fox, a contributor to the support of this society.

Under the Presidency of Dr. Henry Kennon Dunham (Fellow), Cincinnati, Ohio, the National Tuberculosis Association held its thirty-first annual meeting at Saranac Lake, N. Y., June 24 to 27. Many Fellows of the College took part in the program.

Under the Presidency of Dr. Ernest E. Irons (Fellow), Chicago, the second annual meeting and the fourth conference of the American Association for the Study and Control of Rheumatic Diseases was held at Atlantic City, June 10. Half the day was devoted to consideration of chronic arthritis and the other half to rheumatic fever.

Dr. Charles F. Craig (Fellow), New Orleans, La., has been elected President of the American Academy of Tropical Medicine for 1935 to 1936.

Dr. Earl B. McKinley (Fellow), Washington, D. C., was reëlected Secretary.

Dr. Louis H. Fligman (Fellow), Helena, Mont., has been appointed Vice-President of the Montana State Board of Health.

Dr. T. Grier Miller (Fellow), Dr. Richard A. Kern (Fellow) and Dr. Charles C. Wolferth (Fellow), formerly Assistant Professors, have been advanced to fill three new Clinical Professorships established at the University of Pennsylvania School of Medicine.

Dr. Truman G. Schnabel (Fellow) has been advanced from Assistant Professor of Medicine to an Associate Professorship.

A portrait of Dr. Martha Tracy (Fellow), Dean of the Woman's Medical College of Pennsylvania, has been presented to the College on its eighty-fifth anniversary and the twenty-fifth anniversary of Dr. Tracy's connection with the College. The presentation was made by Dr. Ellen C. Potter (Fellow), of Trenton, N. J. Dr. Tracy was personally presented with an automobile by the trustees, faculty, students and friends of the College.

Dr. Lewellys F. Barker (Fellow), Professor Emeritus of Medicine, Johns Hopkins University School of Medicine, delivered the Abner Wellborn Calhoun Lecture on the "Treatment by the General Practitioner of the More Common Diseases of the Nervous System," in connection with the annual meeting of the Medical Association of Georgia at Atlanta, May 7 to 10.

Among Fellows of the College who have delivered lectures during the months of May and June in connection with the Ballin Memorial Lectures at the North End Community Clinic, Detroit, were Dr. Solomon Strouse (Fellow), Chicago, "Obesity and Malnutrition, Their Causes and Management"; Dr. Robert C. Moehlig (Fellow), Detroit, "Pituitary Disturbances"; Dr. Hugo A. Freund (Fellow), Detroit, "Thyroid Disturbances"; Dr. I. M. Rabinowitch (Fellow), Montreal, "Newer Views in the Diagnosis and Treatment of Diabetes Mellitus."

Dr. Marcus W. Newcomb (Fellow), Browns Mills, N. J., was inducted as President of the Medical Society of New Jersey at its one hundred and sixty-ninth annual meeting at Atlantic City, recently.

OBITUARIES

DR. HENRY AARON NORDEN

Dr. Henry Aaron Norden (Fellow), of Fort Wayne, Ind., and Chicago, Ill., died May 1, 1935, of hemiplegia, hypertension and arteriosclerosis.

Dr. Norden was born in New York City in 1867, but later removed to Chicago, where he received his preliminary education under private tutors and his medical training at the Rush Medical College, from which he graduated in 1889. Although he had been retired from active practice of medicine for some time, he was formerly attending physician to the Cook County Hos-

pital, Chicago, Superintendent of the Winfield Tuberculosis Sanatorium, Chicago, Consulting Physician to the Chicago Municipal Sanatorium and Professor of Chest Diseases and Junior Dean of Loyola University School of Medicine. At one time he was the School Health Officer of the City of Chicago. He had been a Fellow of the American College of Physicians since 1919.

DR. JAMES HUNT ROYSTER

Dr. James Hunt Royster (Fellow), born at Townsville, North Carolina, June 29, 1892, died at his home at Richmond, Virginia, March 22, 1935. He was the son of the late Dr. Thomas S. Royster and Sally Alston Royster. His early education was received in the private schools in his county and he was graduated from the Warrenton, North Carolina, High School in 1909. He entered the University of North Carolina, from which he was graduated with the degrees of Bachelor of Arts and Master of Arts in 1913. He entered the Medical College of Virginia that same year, where he pursued his studies for two years, transferring to the Jefferson Medical College in Philadelphia, receiving his medical degree in 1917. He immediately was commissioned as Lieutenant—Junior grade, in the United States Navy, in which service he remained until 1921. He spent practically the entire duration of the war in foreign waters. At the expiration of the war he returned to the Brooklyn Naval Hospital where he remained on duty until his discharge from the service in 1921. Shortly after his return from overseas, he was promoted to the rank of Lieutenant—Senior grade, in the United States Navy.

Dr. Royster had always been interested in psychiatry, and made a special study of it during his service in the Navy. Thus, in 1921 he was appointed associate chief of staff at the Westbrook Sanatorium in Richmond, Virginia, which institution he served until his death.

He was a member of the Governor's Advisory Board of Mental Hygiene. He belonged to the Richmond Academy of Medicine, the Medical Society of Virginia, the Southern Medical Association and the American Medical Association. In 1930 he was made a Fellow of the American College of Physicians. He was a member of the Pi Kappa Alpha Fraternity and the Phi Chi Medical Fraternity. At the time of his death he was Vice-Chairman of the section of Neurology and Psychiatry of the Southern Medical Association.

He is survived by his wife, Mrs. Louise Moss Royster of Richmond, Virginia, his brother, Dr. Thomas S. Royster of Henderson, North Carolina, and two sisters, Mrs. William B. Tarrey of Townsville, North Carolina, and Mrs. Salley Royster Vaughan of Wilson Mills, North Carolina.

Dr. Royster's large circle of friends will mourn his death. He was a loyal friend and greatly beloved by all those with whom he came in contact.

FINLEY GAYLE, F.A.C.P.

DR. WALTER FORD HENDERSON

Dr. Walter Ford Henderson (Fellow), born January 3, 1892, near Shreveport, La., died at New Orleans, April 18, 1935.

Dr. Henderson was graduated from Millsaps College, Jackson, Miss., in 1912. He received his medical degree from Vanderbilt University Medical School in 1916.

From August 1917, until June 1918, he served as Lieutenant in the Medical Corps of the United States Army at Fort Riley, Kansas, at which time he was honorably discharged on account of physical disability.

Following this he practiced medicine at Shreveport, La., and at DeRidder, La. In 1921 he began the intensive study of Roentgenology, pursuing postgraduate work at Tulane University, Johns Hopkins Hospital and the University of Michigan. He later became Director of the Roentgen-Ray Department of the Baptist Hospital in Jackson, Miss. In 1925 he became Director of the Roentgen-Ray Department of Touro Infirmary in New Orleans. In December 1932, he resigned from the Touro Infirmary to go to the Mayo Clinic for an operation for gastric ulcer.

After recovery he returned to Jackson, Miss., May 1933, again to become the Director of the Roentgen-Ray Department at the Baptist Hospital, which position he held until his death.

Dr. Henderson was a member of the Central Medical Society, Orleans Parish Medical Association, New Orleans Gastro-Enterological Society, Mississippi State Medical Society, Louisiana State Medical Association, Southern Medical Association, American Medical Association and the Radiological Society of North America. He was also a member of the Phi Rho Sigma Medical Fraternity and the Kappa Alpha Social Fraternity. He was President of the Mississippi Art Association and a member of the Executive Committee of the New Orleans Art Association. He became a Fellow of The American College of Physicians in 1928.

EXCERPTS FROM MINUTES OF THE MEETINGS OF THE BOARD OF REGENTS

PHILADELPHIA, PA.

April 28, 1935

The first meeting of the Board of Regents, in connection with the Nineteenth Annual Clinical Session of the American College of Physicians, was held at Philadelphia, April 28, 1935, presided over by the President, Dr. Jonathan C. Meakins, with the following members of the Board present: Dr. Jonathan C. Meakins, Dr. James Alex. Miller, Dr. Randolph Lyons, Dr. James F. Churchill, Dr. William D. Stroud, Dr. David P. Barr, Dr. Arthur R. Elliott, Dr. James B. Herrick, Dr. Clement R. Jones, Dr. S. Marx White, Dr. Walter L. Bierring, Dr. John H. Musser, Dr. O. H. Perry Pepper, Dr. Francis M. Pottenger, Dr. Luther F. Warren, Dr. Roger I. Lee, Dr. Sydney R. Miller, Dr. George Morris Piersol, Dr. G. Gill Richards, Dr. Ernest B. Bradley, and the Executive Secretary, Mr. E. R. Loveland.

After reading of the Minutes of the previous meeting of the Board, and approval thereof, the Executive Secretary presented the communications.

Dr. O. H. Perry Pepper presented a recommendation that the College omit the word "Clinical" in the name of the annual meeting, giving as his reasons, first, that this is the only meeting the College holds, and, second, that it is not wholly clinical, and, third, that the present title would indicate a program of clinical sessions only.

On motion by Dr. Pottenger, seconded by Dr. Herrick, and regularly carried, it was

RESOLVED, that in the future the annual meeting shall be known as "Annual Session of the American College of Physicians."

The following resignations, acted upon separately, by resolution, were accepted:

Fellow:

Dr. Arthur W. Grace, New York, N. Y.

Associates:

Dr. Bernard T. Brown, Cazenovia, N. Y.
Dr. John R. Claypool, Mt. Vernon, Ohio
Dr. Albert J. Michels, East Liverpool, Ohio
Dr. Daniel B. Street, Jersey City, N. J.

Ten cases involving fees and dues of Fellows and Associates were presented and individually acted upon.

On motion by Dr. Ernest B. Bradley, seconded by Dr. S. Marx White, and regularly carried, it was

RESOLVED, that in order to expedite the handling of special cases pertaining to resignations, fees and dues, in the future, the Executive Secretary shall present all such communications to one of the standing committees, to be designated by the President, and that that Committee shall bring in its recommendations to the Board of Regents.

Dr. Harry Brandman (Associate), Whiting, Indiana, was discontinued from the Roster for failure to take up election in accordance with provisions of the By-Laws.

In the absence of the Secretary-General, Dr. William Gerry Morgan, because of illness, President Meakins presented his report, including, among other matters, the report of the death of 18 Fellows and nine Associates since the 1934 Session. Deaths not previously reported to the Board were:

Fellows:

Dr. E. Rodney Fiske, New York, N. Y.	December 19, 1934
Dr. Edgar Moore Green, Easton, Pa.	March 9, 1935
Dr. J. R. Morrison, Louisville, Ky.	January 8, 1935
Dr. James Hunt Royster, Richmond, Va.	March 22, 1935
Dr. Harry S. Wagner, Pocasset, Mass.	February 8, 1935

Associates:

Dr. William S. Hannah, Montgomery, Ala.	March 22, 1935
Dr. H. D. Lawhead, Woodland, Calif.	November 29, 1934
Dr. Kenneth G. Mowat, Buffalo, N. Y.	January 13, 1935
Dr. James E. Campbell Taylor, Columbus, Ohio	December 13, 1934
Dr. Stephen L. Taylor, Sherrill, N. Y.	January 29, 1935

President Meakins presented a report on Life Membership, indicating that the list of Life Members had increased considerably since the 1934 Session, and that there had been a larger number added to the Life Membership Roster during the past year than during any previous year. There are at this time 49 Life Members, of which the following 11 are new:

Dr. Henry I. Klopp, Allentown, Pa.
Dr. Ralph O. Clock, New York, N. Y.
Dr. Charles F. Morsman, Hot Springs, S. D.
Dr. Lawrason Brown, Saranac Lake, N. Y.
Dr. Grant O. Favorite, Philadelphia, Pa.
Dr. James Alex. Miller, New York, N. Y.
Dr. Edward C. Klein, Jr., Newark, N. J.
Dr. Joseph M. King, Los Angeles, Calif.
Dr. William J. Stapleton, Jr., Detroit, Mich.
Dr. George Edwin Baxter, Chicago, Ill.
Dr. Clifford E. Henry, Minneapolis, Minn.

A general report on the Philadelphia Session was made by President Meakins and the Executive Secretary.

Dr. George Morris Piersol, Chairman of the Committee on Credentials, reported that his Committee had met at the College Headquarters in Philadelphia on March 30, 1935, and had examined the credentials of 68 candidates for Fellowship and 115 candidates for Associateship. At another meeting of the Committee on April 28, the Committee had examined the credentials of 35 candidates for Fellowship and 70 candidates for Associateship.

Upon motion by Dr. Piersol, on behalf of the Committee on Credentials, seconded by Dr. G. Gill Richards, and regularly carried, it was

RESOLVED, that the following candidates be and herewith are elected to Fellowship in the American College of Physicians.

(There were 82 candidates whose names already have appeared in the College News Notes Section of the May Issue of this journal.)

On motion by Dr. Piersol, on behalf of the Committee on Credentials, seconded by Dr. O. H. Perry Pepper, and regularly carried, it was

RESOLVED, that the following candidates be and herewith are elected to Associateship in the American College of Physicians.

(There were 151 candidates whose names already have appeared in the College News Notes Section of the May Issue of this journal.)

On motion by Dr. James Alex. Miller, seconded by Dr. Musser, and regularly carried, it was

RESOLVED, that the Committee on Credentials adopt a feasible plan in the future for presenting to the Board of Regents in advance a list of the recommendations, both for Fellowship and Associateship, so that the reading of the list would be unnecessary, and individual members of the Board would be ready to take immediate action without unnecessary discussion and consequent delay.

Dr. George Morris Piersol further reported that the Committee on Credentials, through communication with the Surgeon Generals of the U. S. Army and U. S. Navy, had established the following criteria, which are considered very satisfactory to the College, for the selection of men for Associateship and Fellowship:

"Officers of the Medical Corps of the U. S. Army and of the U. S. Navy shall be nominated in each instance by the Surgeon General of the Service concerned, as is the present practice, a method that assists in maintaining the high morale and efficiency of the two medical Services. In making nominations, the Surgeon Generals are in entire accord with the importance of presenting only the names of such men as will be a credit to the American College of Physicians, and who, by the character of their professional work and their experience in the medical field, fully meet the requirements for Associateship and Fellowship.

"Eligibility for Associateship in the American College of Physicians shall be limited to Officers who have had a minimum of five years of military or naval service, with ample clinical experience in internal medicine, laboratory work, or roentgenology, and eligibility for Fellowship shall be limited to Officers who have had a minimum of ten years of military or naval service, with broad experience under qualified supervision in the field of internal medicine, laboratory work, or roentgenology.

"However, there are a few Senior Officers of extensive experience in internal medicine in both Services who may be nominated for initial appointment as Fellows, without passing through the grade of Associate, provided the Surgeon General of the Service concerned fully

sets forth their special qualifications at the time they are nominated. The number available for such exceptional consideration is limited, and their nomination will be presented during the current calendar year."

April 30, 1935

The second meeting of the Board of Regents of the American College of Physicians was held in the Philadelphia Municipal Auditorium, Tuesday, April 30, with President Jonathan C. Meakins presiding, the Executive Secretary, Mr. E. R. Loveland, acting as Secretary, and with the following present: Dr. Jonathan C. Meakins, Dr. James Alex. Miller, Dr. James H. Means, Dr. Randolph Lyons, Dr. James F. Churchill, Dr. William D. Stroud, Dr. David P. Barr, Dr. Arthur R. Elliott, Dr. James B. Herrick, Dr. Clement R. Jones, Dr. S. Marx White, Dr. Walter L. Bierring, Dr. John H. Musser, Dr. O. H. Perry Pepper, Dr. Francis M. Pottenger, Dr. Luther F. Warren, Dr. William J. Kerr, Dr. Roger I. Lee, Dr. Sydney R. Miller, Dr. George Morris Piersol, Dr. G. Gill Richards, Dr. Ernest B. Bradley and Dr. Maurice C. Pincoffs.

Dr. O. H. Perry Pepper, Chairman of the Committee on Examinations, presented the following report:

"The Committee unanimously is of the opinion that the College should at once take steps toward assuming leadership in the field of the certification of Internists. To this end it recommends to the Board of Regents the following:

"1. The establishment with the Section on the Practice of Medicine of the American Medical Association of an 'American Board for the Certification of Internists conducted by the American College of Physicians and the Section on the Practice of Medicine of the American Medical Association.' This Board to consist of nine members: six to be appointed by the College and three by the Section on the Practice of Medicine of the American Medical Association. Additional members representing other appropriate bodies may be added in the future.

"This Board shall be organized and shall function in accordance with the action of the House of Delegates of the American Medical Association in June, 1934, under the heading 'Essentials for Examining Boards in Specialties.' The rules for qualification of candidates then approved shall be enforced by this Board.

"This Board shall seek the approval of the Council on Medical Education and Hospitals of the American Medical Association according to the resolution of that body on October 27, 1934. In order to obtain such approval the Board must present to that body 'satisfactory evidence of the reliability of their procedure in the examination and certification of candidates' and of the acceptance of the standards adopted by the House of Delegates of the American Medical Association.

"This Board shall be financed from the fees collected, but until such time as this is possible, it shall be financed by loans from the College of Physicians. These loans shall be authorized by the Board of Regents up to a limit of $10,000 for the first year. Proper expenses for this Board will include traveling and hotel expenses of members; secretarial and office expenses.

"It is assumed that upon approval of the Board by the Section on the Practice of Medicine of the American Medical Association and by the Council on Medical Education, the Board will proceed as expeditiously as possible to carry out its function as an examining body for the certification of Internists. Upon its supplying a list of certified Internists to the American Medical Association it is assumed that that body will in the future clearly designate these individuals as Certified Internists in such a manner as to distinguish them from those who merely limit their practice to Internal Medicine.

"It is further assumed that this Board will consider for certification without examination such present Masters and Fellows of the College as the Board of Regents may after careful review recommend. In this respect it is to be pointed out that for some years Fellowship in our College has constituted the only certification of an Internist in this country and that this certification has been based on very excellent criteria.

"2. As a corollary of the establishment of such a Board for the Certification of Internists the Committee recommends to the Board of Regents that every effort be made to raise the standards for Fellowship in every direction and specifically that from the date of the institution of examinations by the Board no Internist shall be eligible for Fellowship unless certified by the examining board as an Internist with the exception of those at present holding Associate membership. With the further exception that the College reserves the right to elect Fellows 'for cause' in exceptional instances. It shall be the aim of the College to raise its standards until it achieves a position analogous to the Royal College of Physicians. Election as a Fellow should indicate distinctly superior qualifications; even a further examination than that for certification may some day be instituted for Fellowship.

"Those who at present are Associates shall come up for Fellowship under the custom

existing prior to this meeting, but the hope is expressed that as many as possible will become certified as Internists by examination.

"Election to Associateship will continue as at present with, it is hoped, steadily increasing standards and after the Examining Board is functioning efficiently with the inclusion of Certification by that Board as a requirement. Associates will still have to qualify for Fellowship within the five year period, and Associates elected after this date will only become eligible to Fellowship after being certified as Internists by the American Board for the Certification of Internists.

"The Committee recommends the adoption of this report, the authorization of the Board and its financial support and the appointment by the President of six Fellows of the College to the Board with instructions that they proceed to organize and function as outlined in this report."

Upon motion by Dr. Pepper, seconded by Dr. G. Gill Richards, and regularly carried, it was

RESOLVED, that the above report of the Committee on Examinations be adopted.

On motion by Dr. James Alex. Miller, Chairman of the Committee on Public Relations, seconded by Dr. James B. Herrick, and regularly carried, it was

RESOLVED, that in view of the fact the Chairman of the Board of Registry of Technicians of the American Society of Clinical Pathologists had requested the endorsement of the American College of Physicians of this Registry and that inasmuch as the Committee on Public Relations of the College had investigated the standing of that Society and found it a splendid, ethical organization and the Board of Registry of Technicians to be serving a very useful purpose of value to physicians generally, a letter to that effect be directed to the Board of Registry, offering the coöperation of this College by bringing this service to the attention of its Fellowship, when suitable opportunity offers.

On motion by Dr. James Alex. Miller, seconded by Dr. Bierring, and regularly carried, it was

RESOLVED, that a letter be written to the President of the United States urging financial support for the Army Medical Library, so that the present retrenchment may be discontinued and the outstanding deficit made up.

Reporting for the Committee on Extension of Postgraduate Education, Dr. F. M. Pottenger, Chairman, said the Committee had met and had approved of the same plan suggested at the last meeting, namely, that the matter of sectional meetings for postgraduate training be left with the Board of Governors for each State to decide what particular form of meeting best meets its requirements.

By resolution, eight Fellows and eight Associates were dropped for delinquency of two years' standing.

By resolution, 11 Associates were dropped from the roll because of failure to qualify for Fellowship in the required period of five years.

Following the report of the Editor of the ANNALS OF INTERNAL MEDICINE, Dr. Maurice C. Pincoffs, a resolution was adopted providing that the office of Associate Editor of the ANNALS OF INTERNAL MEDICINE be established and that a sum not to exceed $1,200 per year be provided for that purpose, the Editor being empowered to nominate to the Committee on the ANNALS the name of an Associate Editor, and the Committee being empowered to accept or reject the nomination.

By resolution regularly adopted, it was

RESOLVED, that it be the policy of the American College of Physicians not to elect persons to membership who are primarily hospital administrators.

May 3, 1935

The third meeting of the Board of Regents was held in the Philadelphia Municipal Auditorium, May 3, 1935, with Dr. James Alex. Miller, newly elected President, presiding, and with the Executive Secretary acting as Secretary of the meeting. The following were present: Dr. James Alex. Miller, Dr. Ernest B. Bradley, Dr. Arthur R. Elliott, Dr. David P. Barr, Dr. Egerton L. Crispin, Dr. William D. Stroud, Dr. Jonathan C. Meakins, Dr. James H. Means, Dr. James B. Herrick, Dr. Charles G. Jennings, Dr. James E. Paullin, Dr. John H. Musser, Dr. Francis M. Pottenger, Dr. Luther F. Warren, Dr. William J. Kerr, Dr. Roger I. Lee, Dr. George Morris Piersol, Dr. G. Gill Richards, Dr. Maurice C. Pincoffs, Dr. Charles Hartwell Cocke, Dr. Charles F. Martin, Dr. Randolph Lyons, and the Executive Secretary, Mr. E. R. Loveland.

A communication from Dr. William W. Cadbury (Fellow), of Canton, China, requesting the College to send a message of greeting, and, if possible, a representative to a conference to be held in Canton, China, November 8, 1935, commemorating the introduction of scientific medicine in China one hundred years ago by Dr. Peter Parker, was referred to the Executive Committee for investigation, with power to act.

For the Finance Committee, Dr. Charles F. Martin, Chairman, reported that the funds of the College were in a gratifying condition, there being a surplus for 1934 of $16,160.07, as against $5,801.06 for 1933 and $10,598.08 for 1932. In accordance with the instructions of the Board of Regents, the funds of the College had been segregated into the Endowment Fund of $55,720.00 and the balance of $84,427.10 apportioned to the General Fund. The income for 1934 was $62,000.00 as compared with $52,000.00 for 1933. The Committee recommended that the resident Governor for the State of Delaware be constituted the corporate agent for the College in the future, in the place of the Corporation Trust Company. The Committee recommended the adoption of the proposed budget of the College for the coming year, adding, however, the additional sum of $1,200.00 for the expenses of the Editorial Board of the ANNALS OF INTERNAL MEDICINE.

Upon motions regularly seconded and carried, the following resolutions were adopted:

RESOLVED, that the report of the Finance Committee be received.

RESOLVED, that the Resident Governor for the State of Delaware, Dr. Lewis B. Flinn, be constituted the corporate agent of the College, due to the present agent having increased its charges out of proportion to the services rendered.

Copies of the financial reports and of the budgets for the coming year were distributed, and the Executive Secretary summarized the salient points. With the addition of the item of $1,200.00 for the Associate Editor, authorized by the Board of Regents at its previous meeting, the total of the 1935 budget was $52,238.82.

Upon motion, seconded and regularly carried, it was

RESOLVED, that the detailed budgets presented be adopted as submitted.

In executive session, the Board unanimously voted an honorarium for each of the permanent employees in the College headquarters in consideration of their devoted service and extra labor.

Dr. William Gerry Morgan, of Washington, was unanimously reëlected Secretary-General of the College for 1935–1936.

Dr. William D. Stroud, of Philadelphia, was unanimously reëlected Treasurer of the College for 1935–1936.

The following Executive Committee was elected for the year 1935–1936:

Dr. James Alex. Miller, *Chairman*
Dr. Ernest B. Bradley
Dr. William Gerry Morgan
Dr. William D. Stroud
Dr. Walter L. Bierring
Dr. Roger I. Lee
Dr. James H. Means
Dr. Maurice C. Pincoffs
Dr. Francis M. Pottenger

In accordance with regulations governing the appointment or election of other Committees, with the exception of the Committee on Examinations and the Committee on Extension of Postgraduate Education, which were discharged with thanks, all other committees were appointed. (The personnel of these new committees may be found by consulting page 10 of the June 1935 Issue of the ANNALS OF INTERNAL MEDICINE.)

The Executive Secretary presented invitations for the 1936 Annual Session from Milwaukee, St. Louis and Detroit. President Miller reported that in company with the Executive Secretary, Mr. Loveland, he had visited St. Louis and Detroit to investigate their facilities. He and the Executive Secretary both described the comparative advantages of the cities extending invitations. After thorough discussion, a vote indicated a preference for Detroit for 1936, and on resolution regularly adopted, the College accepted that City's invitation to hold its Twentieth Annual Session there.

Dr. David P. Barr, Chairman of the Committee on Fellowships and Awards, presented his report, explaining the method of arriving at the Committee's decision on the Fellowship award for the coming year, and announced that after careful consideration, the Committee recommended to the Board of Regents the selection of Dr. Michael J. Lepore. Dr. Lepore, now 24 years old, was born in Italy. He graduated from the University of Rochester and served his internship at the Duke University Hospital, where he is now working. He desires to work with Dr. Peters at Yale University. Dr. Lepore is the author of a number of publications, prepared with and without collaboration, and appears to be a young man of great promise. It was the opinion of the Committee that there is an advantage in selecting a man who represents several institutions of learning, rather than one who is in one place and simply requests support for continued work in that same institution.

Upon motion by Dr. Barr, seconded by Dr. Kerr, and regularly carried, it was

RESOLVED, that the Research Fellowship of $1,800.00 for 1935–1936 be awarded to Dr. Michael J. Lepore.

Upon further motion, seconded and regularly carried, it was

RESOLVED, that this Fellowship should start on July 1, 1935, and that an additional necessary appropriation be made on the budget to take care of the overlapping of two and one-half months with the 1934–1935 Fellowship, which will not expire until September 15, 1935.

Dr. William D. Stroud, Treasurer, submitted the financial reports with the information that the investments of the College have appreciated until they now show a book profit of approximately $3,000.00 over their purchase price of $105,828.00; also that the funds of the College had been, for the first time, partially (15 per cent) invested in stocks, with the idea of protecting the investments against inflation.

On motion by Dr. Barr, seconded by Dr. Kerr, and regularly carried, it was

RESOLVED, that a letter of thanks be forwarded to the Orpheus Club of Philadelphia for the excellent concert it had rendered on the occasion of the College Smoker.

On motion by Dr. William J. Kerr, seconded by Dr. G. Gill Richards, and regularly carried, it was

RESOLVED, that the American College of Physicians make representations to the coming meeting of the Association of American Physicians, acquainting them with the plan of the American College of Physicians for the establishment of a national examining board for the certification of internists, and asking for their comments and coöperation.

Adjournment.

ANNUAL BUSINESS MEETING

The Annual Business Meeting of the American College of Physicians was held in the Philadelphia Municipal Auditorium, May 2, 1935, with President Jonathan C. Meakins presiding, and the Executive Secretary, Mr. E. R. Loveland, acting as Secretary.

The Secretary abstracted the Minutes of the previous meeting, which, upon motion, were approved.

The Chairman announced that due to illness the Secretary-General, Dr. William Gerry Morgan, would be unable to present his report.

The Executive Secretary, Mr. Loveland, was requested to report on the financial condition of the College, due to the Treasurer, Dr. William D. Stroud, being delayed. The full financial reports, there presented, have been published in the May 1935 Issue of the ANNALS.

The Executive Secretary followed this with his own report for the year. He announced that the registration at the Philadelphia Session was the largest in the history of the College, being in excess of 2,400. He reported further that 139 Fellows and 244 Associates had been elected since the last Annual Session; also that out of 54 elected to Associateship in 1929, only 10 had failed to qualify for Fellowship; out of 63 elected to Associateship in 1930, 11 had failed to qualify for Fellowship at this meeting. In regard to members discontinued from the Roster because of delinquency, there were only 11 Fellows and 15 Associates dropped during 1934, and only 8 Fellows and 8 Associates dropped for delinquency in 1935. This he pointed out was considerably less than 1 per cent of the membership, which is somewhat of an index of the loyalty members feel toward the College, and of the tenacity with which they retain their memberships. He reported further that the Executive Offices had handled over 40,000 pieces of mail during the past year, and a total income of about $62,000.00; that there had been 11 new Life Members, bringing the total up to 47 in all, and that during the coming summer a new and revised Directory of all College members would be published. The Executive Secretary thanked the General Chairman, the President of the College and members of the local committees for their help and counsel rendered him in connection with the preparation and conduct of this Annual Session.

Dr. James Alex. Miller was then inducted as President of the College. Dr. Meakins, in introducing Dr. Miller, said, in part,

"It is now my duty, Masters and Fellows, to officially bid you good-bye as your President. I expressed my appreciation last evening, and I can only reiterate that again today. It has been a great honor and a great pleasure to do anything I could for the College. The College has done a great deal for me, and therefore I am not only appreciative but thankful.

"I now have a pleasant duty to perform. I feel like the high priest and the golden bough. I am dead but I hand on the torch to one I know will do the job very much better than I could. He is a man beloved by us all, respected by us all, and admired for his knowledge, his judgment, and what he has done for the medical profession in many of its activities. Therefore it gives me great pleasure to hand over the reins of office to my successor, Dr. James Alexander Miller, of New York."

In response, Dr. Miller said:

"I think it is useless for anyone to try to express adequately the feeling which must come

on such an occasion as this. Fortunately, the procedure of the College gives one a year to become gradually desensitized from the shock which comes to you when you are first designated as President-Elect. So that I can perhaps, without as much perturbation as would otherwise have been the case, try to express in a very few words what this honor means to me and what I hope I may be able to do for the College.

"It is an extraordinary body of men which we represent, and to be elected to be its presiding officer is an honor second to none, and I appreciate it very much. To follow after those who have gone before is a privilege, but also an overwhelming responsibility. I know that I will not be able to do as well as they, but all that I can say is that my very deepest sympathy is with the interest of the College, and to the utmost of my ability I will do my best to keep on carrying the torch of the College of Physicians in the way that it has been so magnificently carried before.

"I think that we have a great future before us, as well as a magnificent past, and I hope as we go on together that we may, officers and Fellows alike, achieve much that is now in our hearts in the way of hope as well as well earned satisfaction with what has gone before.

"I know that no President of this organization can achieve anything excepting with the support and hearty coöperation of all the Fellowship, all the Governors, and the Regents, and particularly, may I say, of the Executive Office, and I think we have an organization in all of these departments of which we are very proud, and upon which I know that I as your presiding officer for the time being will be able to rely with the fullest of confidence. I hope that we will make further progress and I trust that I may during the coming year at least not allow the standards which we have set up to be lowered. I thank you from the bottom of my heart."

President Miller then introduced Dr. George Morris Piersol, who presented a gavel to the retiring President, Dr. Meakins, as a token of the esteem of the College.

Dr. Charles F. Martin, Chairman of the Committee on Nominations, presented the following report:

"The Committee on Nominations, appointed by your President, in accordance with the By-Laws, presents the following nominations:

A. For the Elective Officers:

President-Elect ..... Dr. Ernest B. Bradley, Lexington, Ky.
First Vice President ..... Dr. Arthur R. Elliott, Chicago, Ill.
Second Vice President ..... Dr. David P. Barr, St. Louis, Mo.
Third Vice President ..... Dr. Egerton L. Crispin, Los Angeles, Calif.

B. For the Board of Regents, term expiring 1938:

Dr. Jonathan C. Meakins, Montreal, Que.
Dr. James H. Means, Boston, Mass.
Dr. James B. Herrick, Chicago, Ill.
Dr. Charles G. Jennings, Detroit, Mich.
Dr. James E. Paullin, Atlanta, Ga.

C. For the Board of Governors, term expiring 1938:

Dr. James F. Churchill ..... (Southern) California, San Diego
Dr. Gerald B. Webb ..... Colorado, Colorado Springs
Dr. Henry F. Stoll ..... Connecticut, Hartford
Dr. Wallace M. Yater ..... District of Columbia, Washington
Dr. Ernest E. Laubaugh ..... Idaho, Boise
Dr. Samuel E. Munson ..... (Southern) Illinois, Springfield
Dr. Robert M. Moore ..... Indiana, Indianapolis
Dr. Thomas Tallman Holt ..... Kansas, Wichita
Dr. William B. Breed ..... Massachusetts, Boston
Dr. Adolph Sachs ..... Nebraska, Omaha
Dr. Allen A. Jones ..... (Western) New York, Buffalo
Dr. Leander A. Riely ..... Oklahoma, Oklahoma City
Dr. Edward J. G. Beardsley ..... (Eastern) Pennsylvania, Philadelphia
Dr. E. Bosworth McCready ..... (Western) Pennsylvania, Pittsburgh
Dr. J. Owsley Manier ..... Tennessee, Nashville
Dr. Louis E. Viko ..... Utah, Salt Lake City
Dr. Jabez H. Elliott ..... Ontario, Toronto, Canada
Dr. William M. James ..... Panama and the Canal Zone

(Term expiring 1937)

Dr. C. W. Dowden ..... Kentucky, Louisville
Dr. Glenville Giddings ..... Georgia, Atlanta
Dr. Ramon M. Suarez ..... Puerto Rico, San Juan

Respectfully submitted by

Committee on Nominations

Dr. Charles F. Martin, *Chairman*
Dr. Roger I. Lee,
Dr. William J. Kerr,
Dr. Charles H. Cocke,
Dr. Gerald B. Webb."

Upon motion duly seconded, the report of the Nomination Committee was adopted unanimously, and the persons named declared duly and unanimously elected.

Dr. S. Marx White presented the following report for the Committee on Resolutions:

"I move that an expression of appreciation be spread on the Minutes to recognize the extraordinary character of the Session provided in this cradle of medical education in America, and that special mention be made of the service of Dr. Alfred Stengel, Chairman, and his Committee on Arrangements; Dr. O. H. Perry Pepper, Chairman, and his Committee on Clinics; Dr. Thomas Fitz-Hugh, Jr., and the Committee on Morning Lectures; Dr. Robert G. Torrey and the Committee on Auditorium; Dr. Richard A. Kern and the Committee on Publicity; Dr. Harry B. Wilmer, the Orpheus Club, and the Entertainment Committee; Mrs. George Morris Piersol, Chairman of the Committee on Entertainment of Visiting Women; as well as the medical profession of Philadelphia represented by the Philadelphia College of Physicians and the Philadelphia County Medical Society; also, the Convention Bureau of the Chamber of Commerce."

The motion was seconded and carried unanimously.

There being no further business, the meeting adjourned at 5:10 p.m.